

与断奶仔猪肠道健康和发育 相关的的饲料和添加剂

Feed- and feed additives-related aspects of gut
health and development in weanling pigs

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简介 Today's presentation

1. 胃肠道健康： 前言和概述 Gastrointestinal tract health:
introduction and general comments
2. 蛋白质/氨基酸水平/类型对仔猪断奶后健康和生产性能的影响 Effects of protein /amino acids level / type on health and production after weaning
3. “纤维”在胃肠道健康和发育中的作用 The role of “fibre”
in gastrointestinal health and development
4. 影响胃肠道健康和发育的非日粮机制 Non-dietary
mechanisms that impact on health and development of the gastrointestinal tract
5. 总结 Concluding comments

什么是“健康”的胃肠道？

What is a “healthy” gastrointestinal tract?

1. 最佳的消化功能 Optimal digestive function
2. 最佳的吸收功能 Optimal absorptive function
3. 有效的屏障功能 Effective barrier function
4. “稳定的”微生物区系 “Stable” microbiota
5. 高效、低成本的免疫系统 Effective and low cost immune system

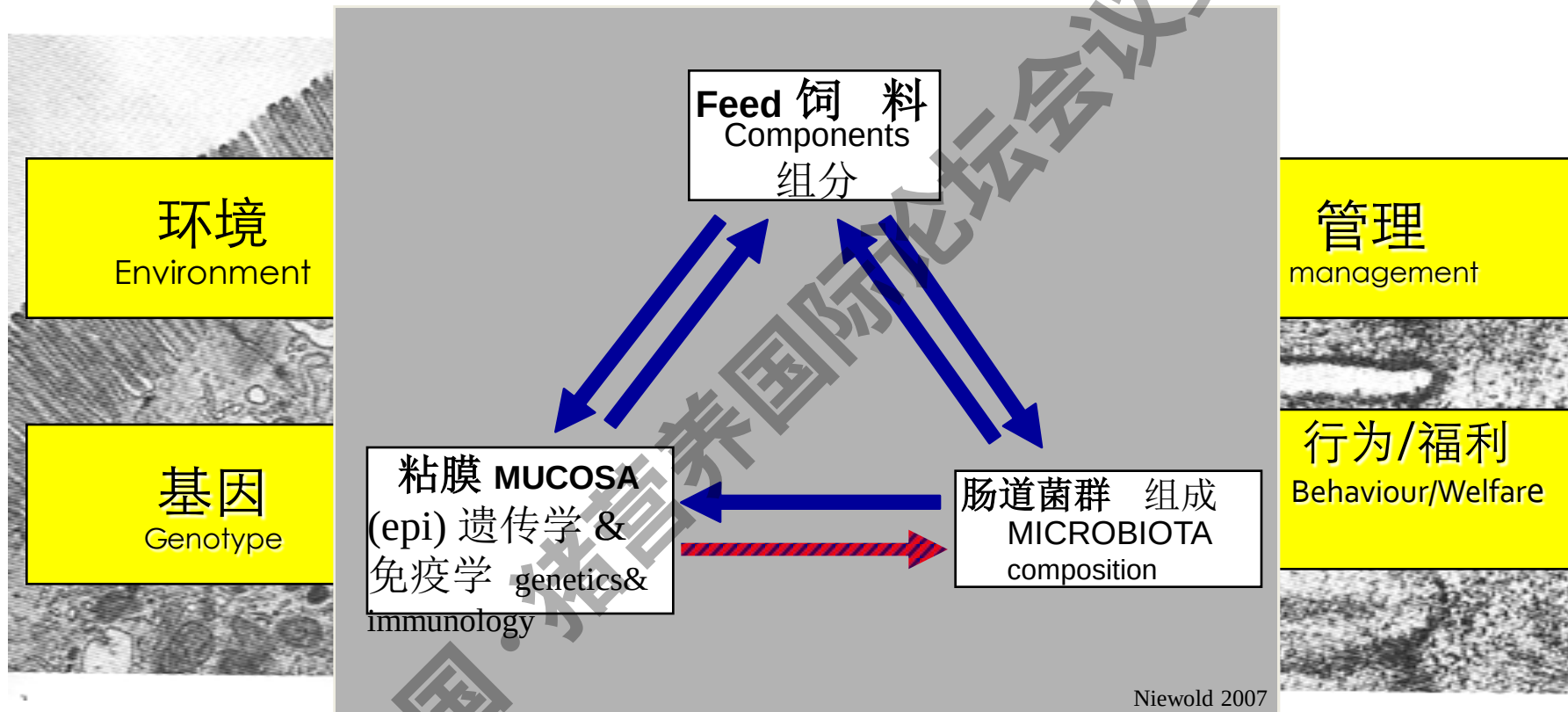
免疫系统的激活水平对6-27 kg LW 生产性能的影响

Level of immune system activation affects performance 6-27 kg LW

Item 项目	Immune system activation 免疫系统激活	Dietary lysine, % of the diet 日粮赖氨酸(%)			
		0.60	0.90	1.20	1.50
Daily gain, grams 日增重, 克	Low 低	400	556	644	663
	High 高	357	495	510	504
Daily feed intake, grams 日采食量, 克	Low 低	896	1025	1052	1002
	High 高	889	954	889	911
Gain:feed, 肉料比, g/kg	Low 低	445	544	613	662
	High 高	395	522	581	565

什么能维持肠道的健康？

What contributes to a highly functional gut?



维持胃肠道菌群平衡

Maintaining a balanced microbiota in the gastrointestinal tract

- 肠道菌群对宿主消化组织和免疫组织的发育有重要的作用。 The microbiota has essential functions in the development of digestive and immune tissue in the host animal
- 肠道是机体最大的免疫器官，能防止肠道病原菌的侵袭。 The intestine is the biggest immune organ in the body, but to achieve appropriate protection from pathogens a complex gut microbiota is essential
- 致病菌一直存在于肠道中，致病菌与非致病菌的平衡是否被打破决定着是否会发生疾病。 Pathogenic bacteria are always present in the gut, and it is the 'balance' between pathogenic and non-pathogenic bacteria that determines whether or not disease occurs

菌群对肠道免疫系统的影响

Imprinting of the gut immune system by the commensal bacteria microbiota

无菌试验表明，肠道菌群影响多系统功能

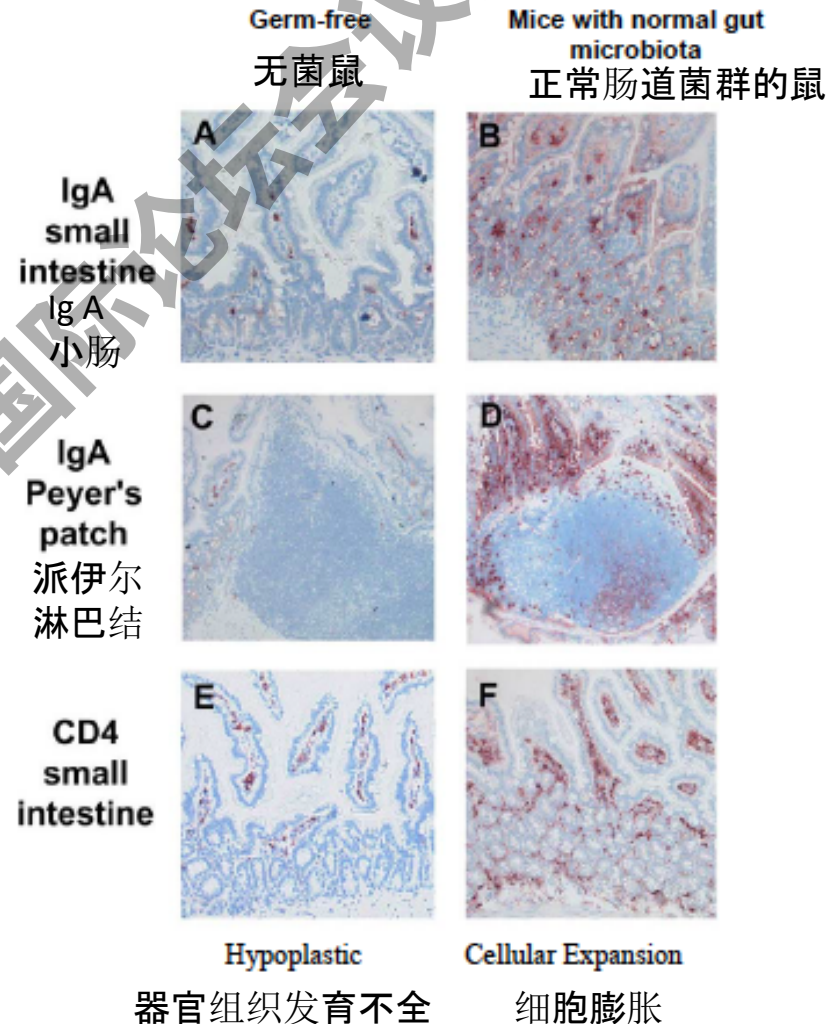
- Experiments with germ-free reveal many different systems are shaped by the microbiota

免疫系统的激活需要大量的菌群

- Stimulation of immune system requires high doses of bacteria

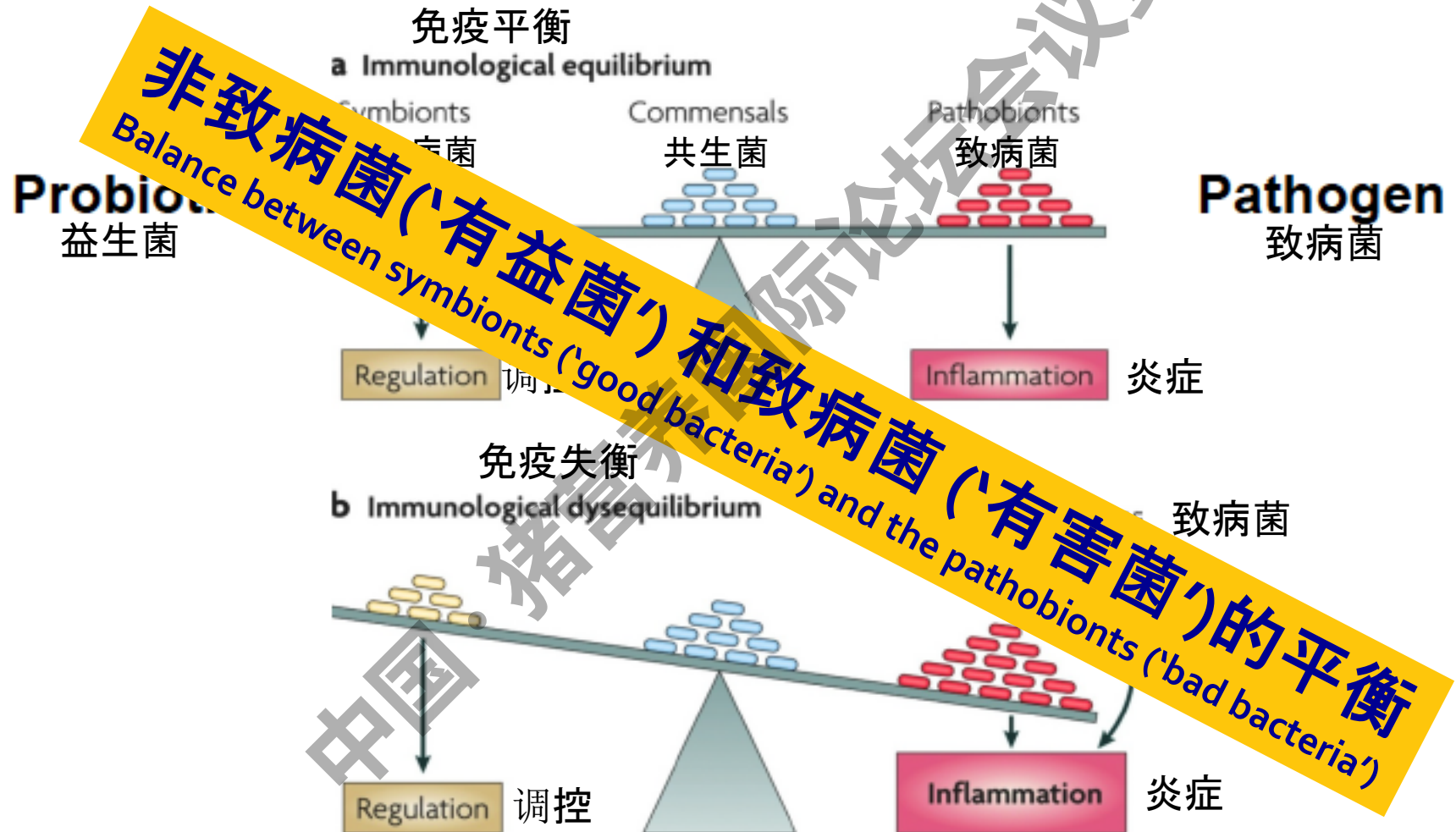
活菌比死菌更能激活免疫系统

- Live bacteria are better stimulus for immune system than dead



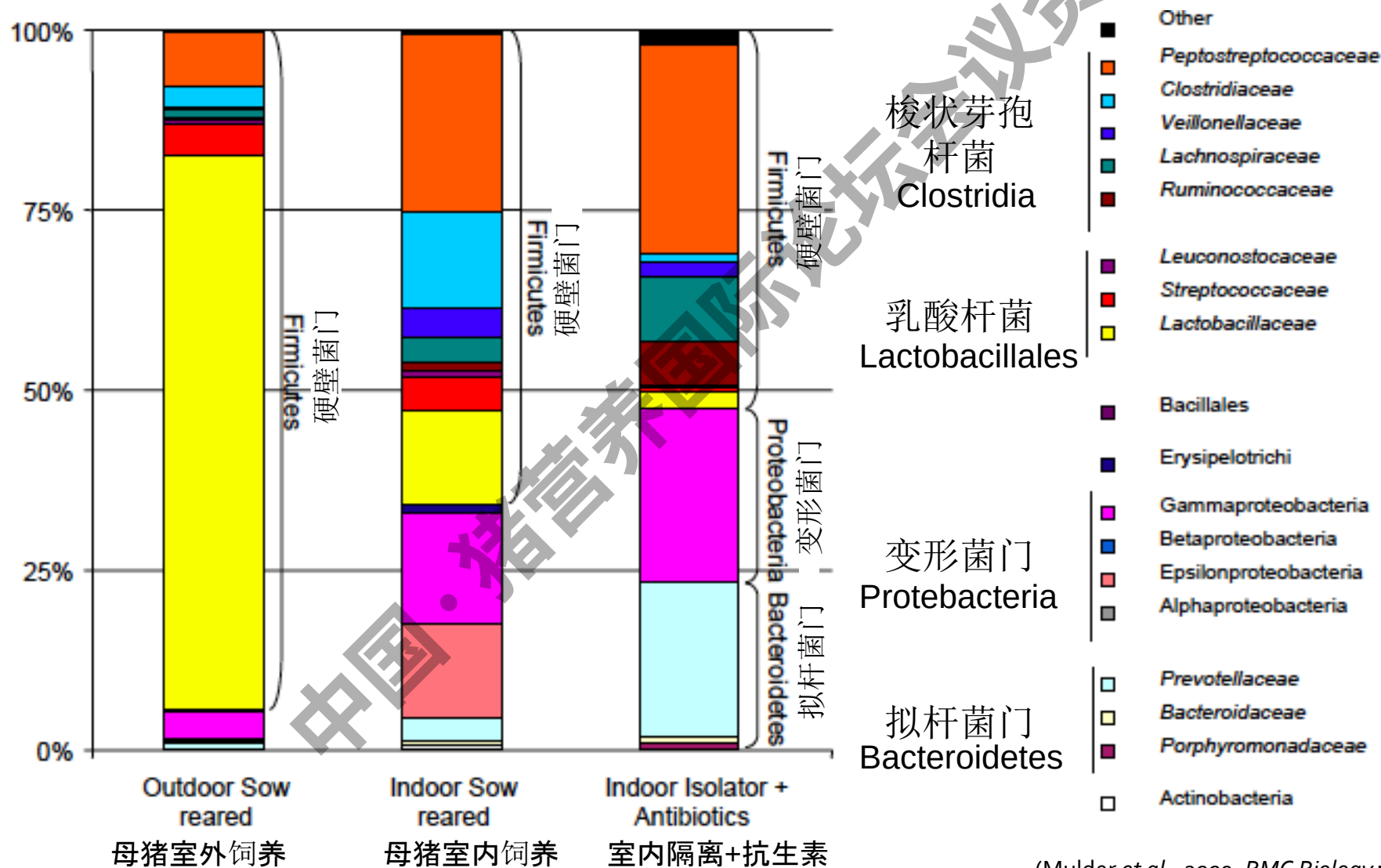
肠道菌群的组成对免疫稳态和平衡的影响

Microbiota composition is essential for immune homeostasis and balance



早期肠道环境改变微生物黏膜菌群相关多样性

Early-life environment alters microbial mucosa-associated diversity



饲料添加剂

Feed additives

中国·猪营养国际研讨会资料

什么是饲料添加剂？

What is a feed additive?

- 饲料添加剂被定义为化学物质、微生物和某种制剂，而不是饲料原料和预混料。这些物质被有意识地添加到饲料或水中，能发挥以下一种或多种功能

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 following functions

- 有助于改善饲料的特性; Favorably affect the characteristics of feed,
- 有助于改善动物产品的特性; Favorably affect the characteristics of animal products,
- 有助于改善观赏鱼类和鸟类的颜色; Favorably affect the colour of ornamental fish and birds,
- 满足动物的营养需要; Satisfy the nutritional needs of animals,
- 有助于改善动物生产对环境的不良影响; Favorably affect the environmental consequences of animal production,
- 有助于改善动物生产，性能和福利，特别影响胃肠道菌群和饲料的消化率; Favorably affect animal production, performance or welfare, particularly by affecting the gastro-intestinal flora or digestibility of feedingstuffs, or
- 有抗球虫剂或组织鞭毛虫抑制剂的作用 Have a coccidiostatic or histomonostatic effect

什么是饲料添加剂？

What is a feed additive?

- **同时，饲料添加剂不应** The feed additive shall *not*:
 - 有对动物健康，人类健康或环境的不利影响， Have an adverse effect on animal health, human health or the environment,
 - 存在误导使用者的行为， Be presented in a manner which may mislead the user,
 - 损害消费者的利益，损害动物产品的特性或误导消费者对动物产品特性的认识（欧盟官方杂志，2003年）。 Harm the consumer by impairing the distinctive features of animal products or mislead the consumer with regard to the distinctive features of animal products
- **除了抗球虫剂和组织鞭毛虫抑制剂外的抗生素不被认为是饲料添加剂** Antibiotics, other than coccidiostats or histomonostats, shall not be authorized as feed additives

(Official Journal of the European Union; 2003)

Health & Science



In the News | Romney tax returns | Chris Christie | Felix Hernandez | Michael J. Fox | Julia Child

Orange Savings Account



消费者调查
显示：无抗
生素肉和家
禽更受欢迎

Antibiotic-free meat and poultry score high in Consumer Reports survey



Bigstock - Antibiotic-free meat and poultry are widely available and score high in Consumer Reports survey.

消费者对动物饲料中抗生素的态度

Consumer attitudes to antibiotics in animal feedstuffs

Testing products since 1936.

Consumer Reports is an expert, independent, nonprofit organization whose mission is to work for a fair, just, and safe marketplace for all consumers and to empower consumers to protect themselves.

- “消费者报告”将消费者送到23个州的13个大型连锁超市的136家分店，去看那些没有饲喂抗生素的肉品和家禽产品在销售，价格是多少。“Consumer Reports” sent shoppers to 136 stores of the 13 largest supermarket chains in 23 states to see what meat and poultry products raised without antibiotics are being sold and for how much
- 2012年3月，他们还对全美1000位当地居民进行了一次全国性调查，主要调查结果包括 They also conducted a nationwide survey of 1,000 U.S. residents in March 2012. Key findings include:
 - 86% 的消费认为当地超市应该供应没有饲喂过抗生素的肉品； 86% of consumers think meat raised without antibiotics should be available in their local supermarket
 - 24%的消费说其当地超市不供应没有饲喂过抗生素的肉品； 24% of consumers said meat raised without antibiotics was not available at their local supermarket;
 - 61%消费表示他们愿意会多支付5美分或更多来买无抗生素肉品或禽肉， 37% 的人甚至表示愿意多支付1美元或更多； 61% of consumers would pay an additional 5 cents or more per pound for antibiotic free meat and poultry; 37% indicated they would pay \$1.00 a pound or more
 - 72%的消费者非常担忧抗生素的广发使用会引起新的超级细菌，这些超级细菌引起的疾病是抗生素无法治愈的； 72% of consumers are very concerned about the widespread use of antibiotics creating new superbugs that cause illnesses that antibiotics cannot cure
 - 消费者信任“有机”商标，因为有机认证明确规定不能在畜牧生产中添加抗生素。其它商标，如“天然”，“无抗生素”，“无抗生素残留”和“无抗生素促进剂”等，都不被信任。 While consumers can trust “organic” labels, since organic certification precludes antibiotic use in livestock, other labels such as “natural,” “antibiotic-free,” “no antibiotic residues,” and “no antibiotic growth promotants” can not be trusted
 - 美国13个大型连锁超市中，Whole Foods是唯一一个只卖没有饲喂抗生素的肉品和禽产品的。 Of the 13 largest U.S. supermarket chains, [Whole Foods](#) is the only chain to sell only meat and poultry raised without antibiotics

media release

2013 IS SET TO BE A HAPPIER NEW YEAR FOR PIGS

Coles today announced it will speed up its plans to implement a sow stall-free policy on its Australian fresh pork and small goods, as well as imported pork products which is not only a win for pig welfare but for consumer choice.

The supermarket giant had originally benchmarked 2014 as the date from which all Coles branded pork, including ham and bacon produced in Australia and overseas, be sourced from pigs not confined in sow stalls. But today it announced it will reach that goal twelve months early, by the start of 2013.

Many Australians have said that they would prefer to buy higher welfare pork and, in order to make a meaningful impact to pig welfare; we need more humanely farmed products available on the supermarket shelf.

"Removing sow stalls is a fantastic step in the right direction and it would be good to see farrowing crates phased out next. That is why the RSPCA supports the Pork CRC's ongoing research into alternative, confinement-free farrowing systems that cater for the welfare needs of both the sow and her piglets.

商品单.... A shopping list....

- CuSO_4 and ZnO
- 益生菌 Probiotics
- 有机酸 (In) organic acids
- 益生素 Prebiotics
- 甘露, 丁酯 & 乳低聚糖
Manno, fructo & galacto-oligosaccharides
- 菊粉, 纤维源 Inulin, fiber sources
- 凝集素(土豆, 大叶野茉莉) Some lectins (tomato, snowbell)
- 几丁质(鱼, 昆虫) Chitins (fish, insect)
- 海带(海带多糖, 褐藻素) Sea weed (Laminarin, fucoidan)
- 精油(药草 & 调味料) Essential oils (herbs & spices)
- β -(1 $\rightarrow$ 3),(1 $\rightarrow$ 6)-葡聚糖(酵母, 细菌)
 β -(1 $\rightarrow$ 3),(1 $\rightarrow$ 6)-glucans (yeast, bacterial)
- 一些氨基酸 Some amino acids
- 一些胺类 Some amines
- 中链甘油三脂 Medium-chain triglycerides
- 酶 Enzymes
- 牛奶蛋白(初乳) 和血浆蛋白
Milk proteins (colostrum) and blood plasma
- ω -3 脂肪酸 ω -3 fatty acids
- L-左旋肉碱 L-carnitine
- 免疫球蛋白 Immunoglobulins
- 抗菌肽 Anti-microbial peptides
- 抗菌病毒 Anti-microbial viruses
- 疫苗/噬菌体
Vaccines/bacteriophages
- 尿酶抑制剂 Urease inhibitors
- 表皮生长因子, 肽 YY,
EGF, peptide YY,
- 核苷酸, 核苷 Nucleotides, nucleosides
- “健康的” 日粮 ‘Healthy’ diets



EAAP 2007 Dublin Ireland
Wednesday 29th August 2007 8.30-12.30

FRH Feed for Pig Health



Feed for Pig Health Industry Workshop

The results from this European Union FP6 funded (€4 million) project researching into the Development of natural alternatives to anti-microbials for the control of pig health and promotion of performance will be presented as four review papers.

Probiotics: Do they have a role in the pig industry?

Marth Kenny, Elena Mengheri and Hauke Smit

- What are probiotics?
- How may they act - what makes a good probiotic?
- Fermented liquid feed
- Recent research in humans and pigs
- Potential practical application

Impact of bioactive substances on the gastrointestinal tract and performance of weaned piglets

J.P. Lalles, P. Bost, P. Janczyk, S.J. Koopmans, D. Torralardona

- Many compounds have potential to influence piglet performance around the time of weaning
- Organic acids may be beneficial. Butyrate has promising effects
- Do supplemental amino acids or spray-dried plasma have beneficial roles?
- What are the considerations when using essential oils as additives?
- Antagonistic interactions between bioactive substances and dietary components have to be considered.

Alternatives to in-feed antibiotics: use of prebiotics in the nutrition of weaning piglets

Pelikaan WF, Bikker P, Verstegen MMA, and Smit H.

- In vitro and in vivo techniques to quantify prebiotic effects in weaned piglets
- Feed ingredients as substrate for microbiota
- Influence of prebiotic effects on microbial activity and gut ecology
- Possible consequences for animal performance and health.

Gut Immunology - or what keeps the outside world out of the organism?

Isabelle P. Oswald, Hermann J. Rothkötter, Mick Bailey and Christopher R. Stokes

- Components and purpose of the pig's immune system
- Development of the immune system - Can we influence this?
- How does the gut epithelium communicate with the immune system?
- Co-culture of intestinal epithelial cell lines and immune cells allows us to study the development of the immune responses to food and bacteria (pathogens and commensals).

Throughout Europe it is normal commercial practice that pigs are weaned at an age much less than that which occurs in the wild. This causes gastrointestinal disturbances and an increased susceptibility to infection, resulting in large economic losses to the pig industry. Whilst it is clear that many interacting factors may play a role in the increased susceptibility to infection current methods of control rely on the very wide use of antibiotics. The aim of this multidisciplinary project was to examine the potential of using plant extracts and other natural substances, not considered harmful for human or animal health, as alternatives to antimicrobials in reducing losses from post-weaning infection, and improving productivity.

It is widely recognised that many interacting factors play a role in this "disease process", we therefore proposed to use four distinct approaches to address these. Specifically to determine the effect of a range of plant extracts, pre-biotics, Lactobacillus fermented feed and feed intake on their ability to reduce the requirement for the use of antibiotics in the post-weaned pig. Plant extracts were evaluated through an initial in vitro screening process and a small representative group selected on the basis of their diverse range of activities. These plant extracts together with the other experimental approaches were characterised for their effect upon specific established indicators of gut health. These included gut physiology, gut immunology, and gut ecology.

How to register

If you are registering for the whole EAAP conference then admission to this workshop is included. If you just wish to register for the Feed for Pig Health workshop the fee is €70. Go to the EAAP 2007 website (<http://www.eaap2007.ie>). Select the Register page and click to register online. Fill in the required details and proceed to the Registration Details page. Select "Satellite Workshops & Symposia Registration Only" (cost €0.00) then proceed to "Satellite Workshops & Symposia Registration". On this page select "Feed For Pig Health Non EAAP Meeting registered delegate" (€70.00). Continue through the rest of the registration pages to finalise your registration and payment.



EAAP 2007

4th Annual Meeting of the European Association for Animal Production
Dublin • Ireland • August 28th - 31st • 2007



调控猪体健康和改善生产性能的天然抗生素替代物的研究进展

The Development of Natural Alternatives to Antimicrobials for The Control of Pig Health and Promotion of Performance

(Project no: FOOD-CT-2004-506144)

Dates: 1/7/2004 - 31/12/2007

抗生素替代物有效性和潜力的研究进展

Efficacy and potential for developing alternative additives and strategies to replace the role of antibiotic feed additives

饲料添加剂替代品种	Alternative feed additives	功效 Efficacy*	发展潜能 Potential for development*
抗生素	Antibiotics	+++++	0
氧化锌	Zinc Oxide	++++	0
硫酸铜	Copper sulphate	+++	0
有机酸	Organic acids	+	0
酶	Enzymes	+++	+++
发酵前和接种	Pre-fermentation and inoculation	?	+
益生菌	Probiotics	+	+
发酵底物(益生菌)	Fermentable substrates (Prebiotics)	++	+++
乳糖	Lactose	++	0
沸石和粘土矿物质	Zeolites and clay minerals	?	0
营养品(人参、牛至油)	Nutraceuticals (e.g. gingseng, oregano)	?	+
分离大豆	Soya isolates	+	+
免疫球蛋白	Immunoglobulins	++	?
表皮生长因子	Epidermal growth factors	?	?
Colostrally源生长因子	Colostrally driven growth factors	?	?
饲养管理技术	Husbandry/management techniques	Efficacy	Potential for development
全进全出	All-in-all production	++++	++++
卫生	Hygiene	++++	+++
推迟断奶	Later weaning	?	+
户外饲养	Outdoor production	+	0
初乳的质量和采食量	Colostrum quality and intake	++	++
免疫	Immunisation	+++	++
饮用水的质量和供应	Drinking water quality and provision	++	+++
所有者和饲养者的教育水平	Education - owner and stockperson	++++	+++++

* - Efficacy and development based on a subjective score 0 (zero) to ++++ (very high), or ? (unknown)

*-功效和潜能用0(没有效果) ++++(效果很好) 由低到高的描述, 或者是?(未知)

(http://www.bsas.org.uk/about_the_bsas/issue_papers/alternatives_to_antibiotic_feed_additives_for_pigs/)

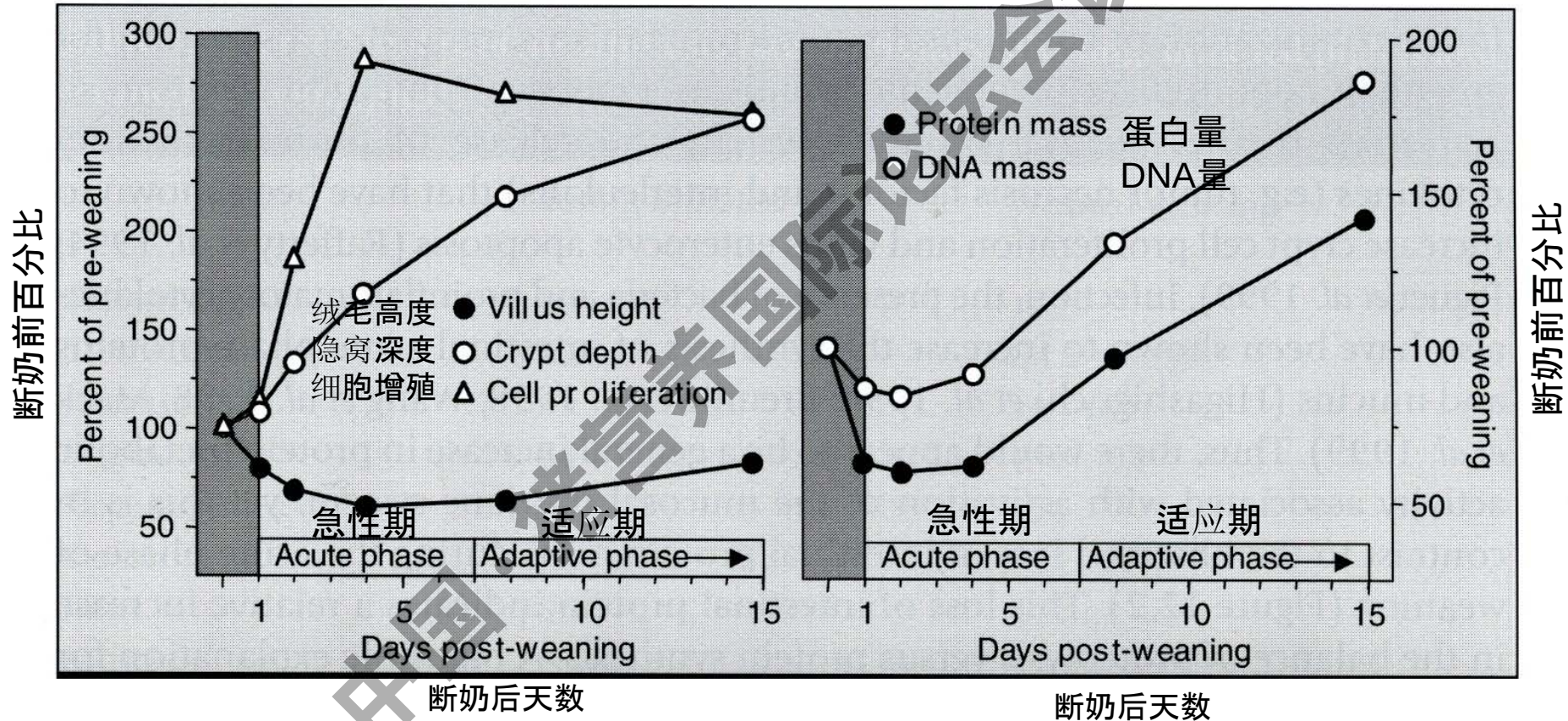
断奶仔猪的胃肠道健康

Gastrointestinal tract health - the weanling pig



断奶后小肠的两个变化阶段

There are two phases of change in the small intestine after weaning



断奶后采食量和肠道屏障功能

Feed intake after weaning and gut barrier function

- 断奶后暂时性饥饿会影响肠道屏障功能 Period of temporary **starvation** after weaning compromises gut barrier function
- 低采食量 Low feed intake,
 - 增加肠上皮淋巴细胞和浸润细胞的数量 Increases numbers of lymphocytes and infiltrated cells in epithelium
 - 引起短暂的炎症反应 Causes a transient inflammatory response
 - 降低肠上皮组织阻力（渗透性增强） Decreases epithelial tissue resistance (more “leaky” intestines)



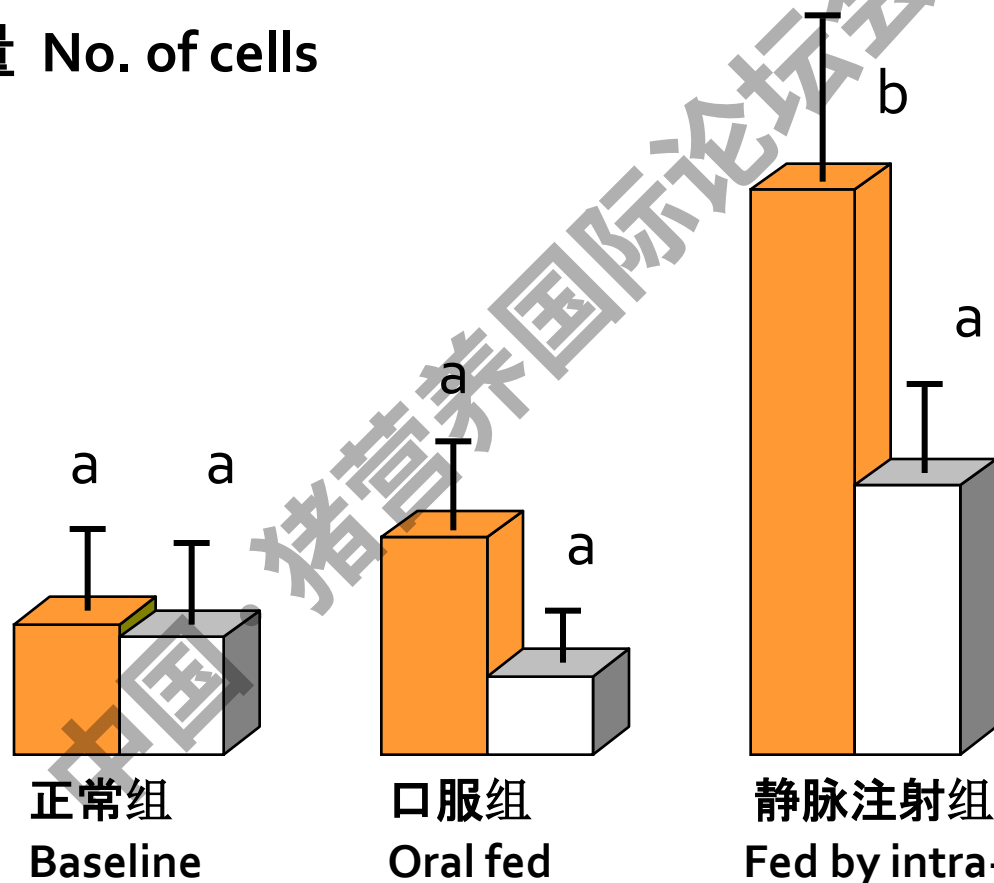
饥饿仔猪绒毛中T淋巴细胞数目增加

T-lymphocyte numbers
increase in the villi of starved piglets

出生后饲喂7天
Pigs fed for
7 d after birth

细胞数量 No. of cells

14
12
10
8
6
4
2
0

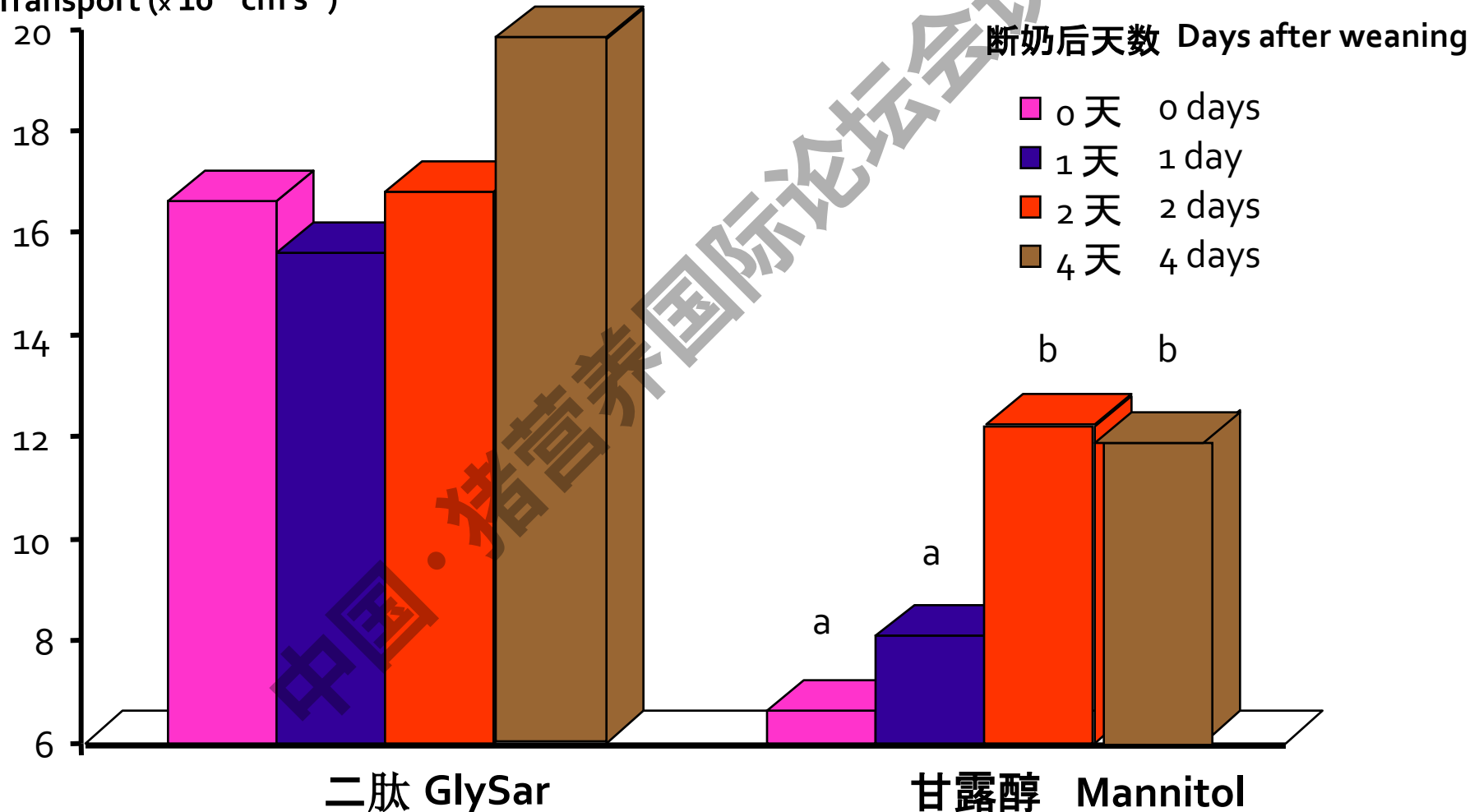


空肠 Jejunum
回肠 Ileum

断奶后肠道上皮跨细胞(二肽)和细胞间 (甘露醇)转运量增加

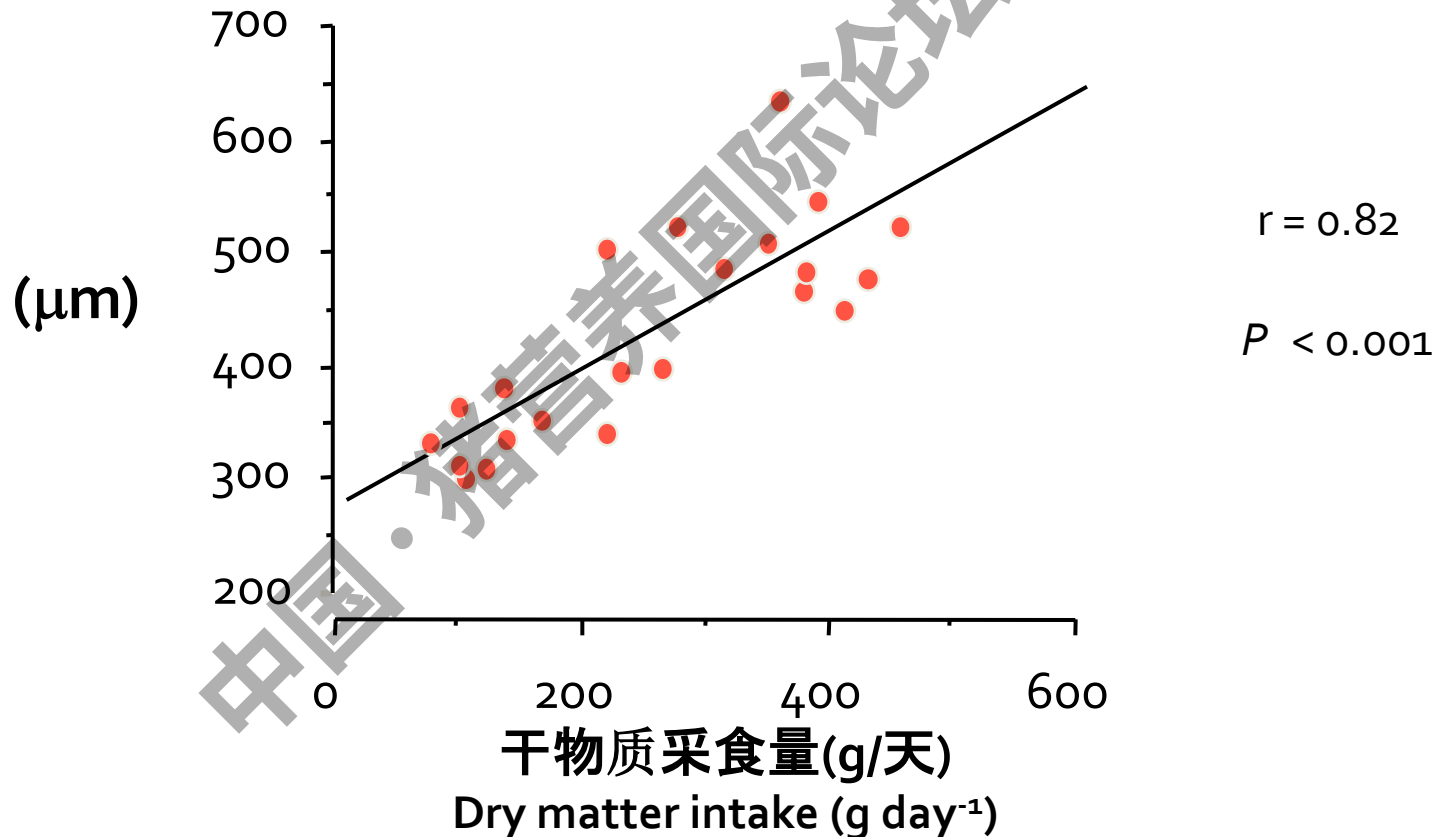
Transcellular (GlySar) and paracellular (Mannitol) transport increase after weaning

转运速率($\times 10^{-6} \text{ cm s}^{-1}$)
Transport ($\times 10^{-6} \text{ cm s}^{-1}$)



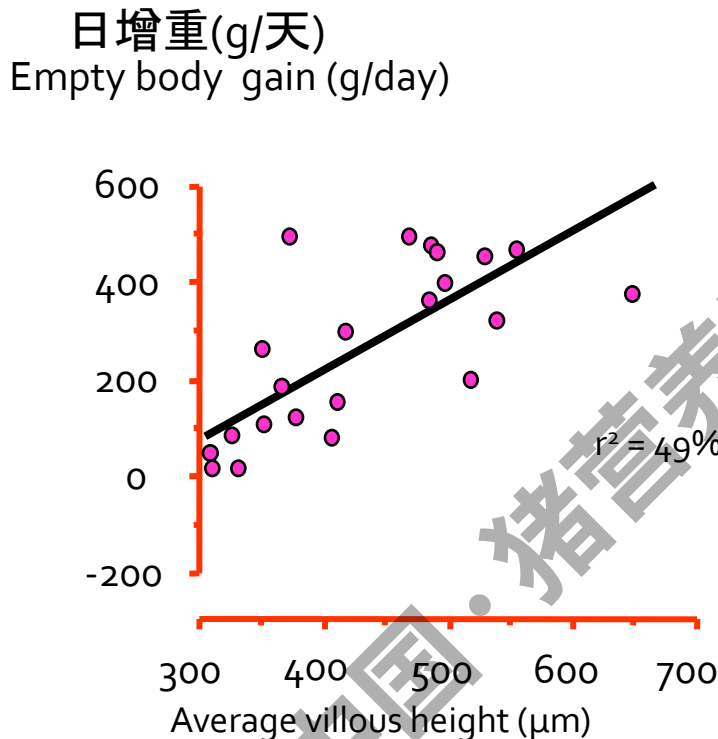
饲喂人工奶仔猪的采食量和 平均绒毛高度

Food intake and average villous height in milk-fed pigs

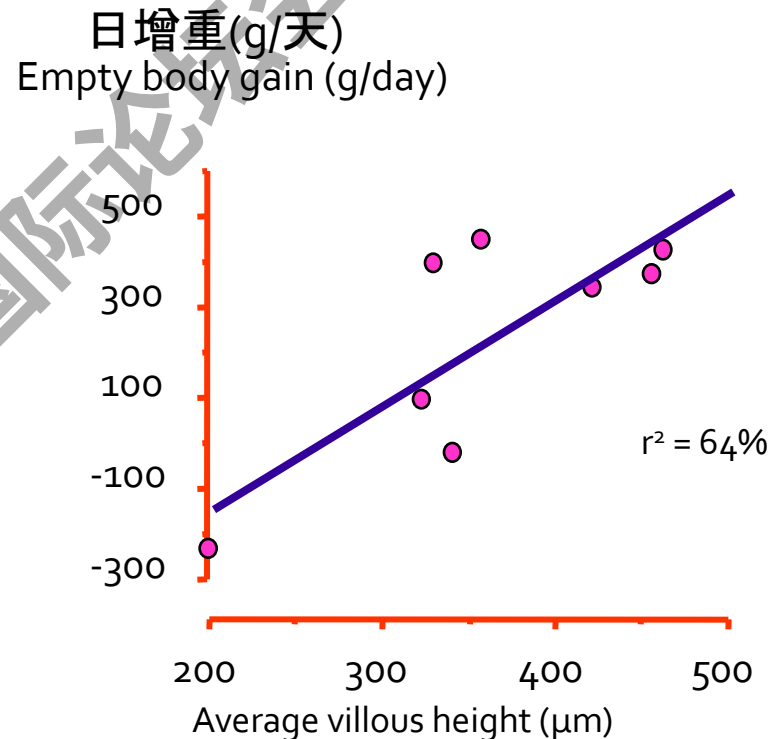


断奶后仔猪的绒毛高度决定 空腹日增重

Villous height determines empty body weight gain after weaning



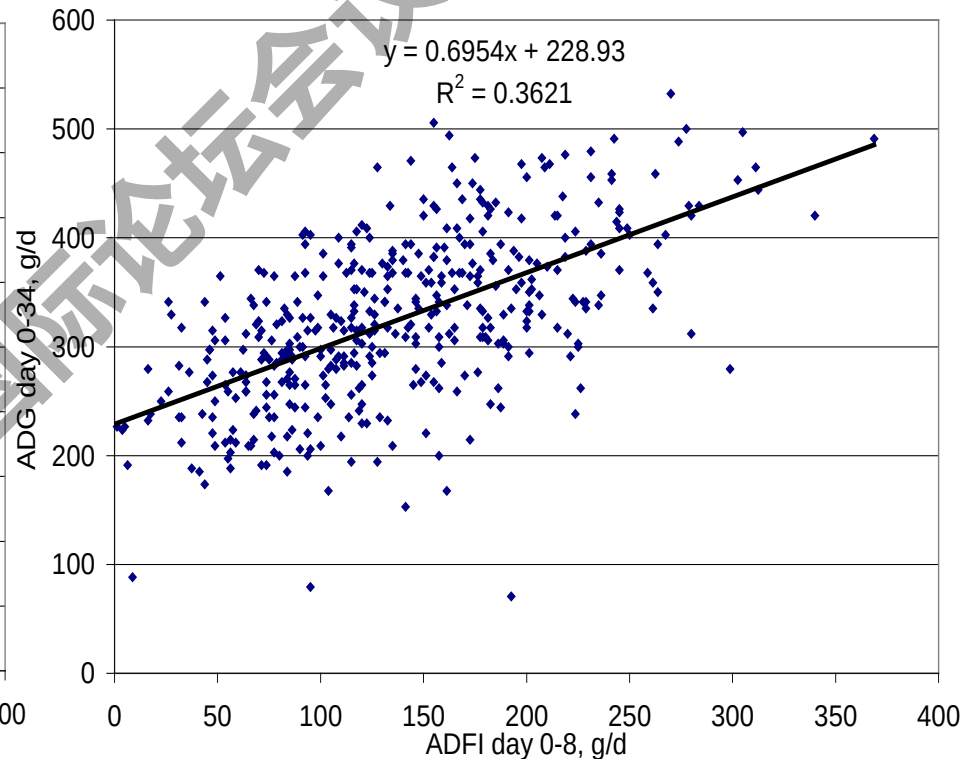
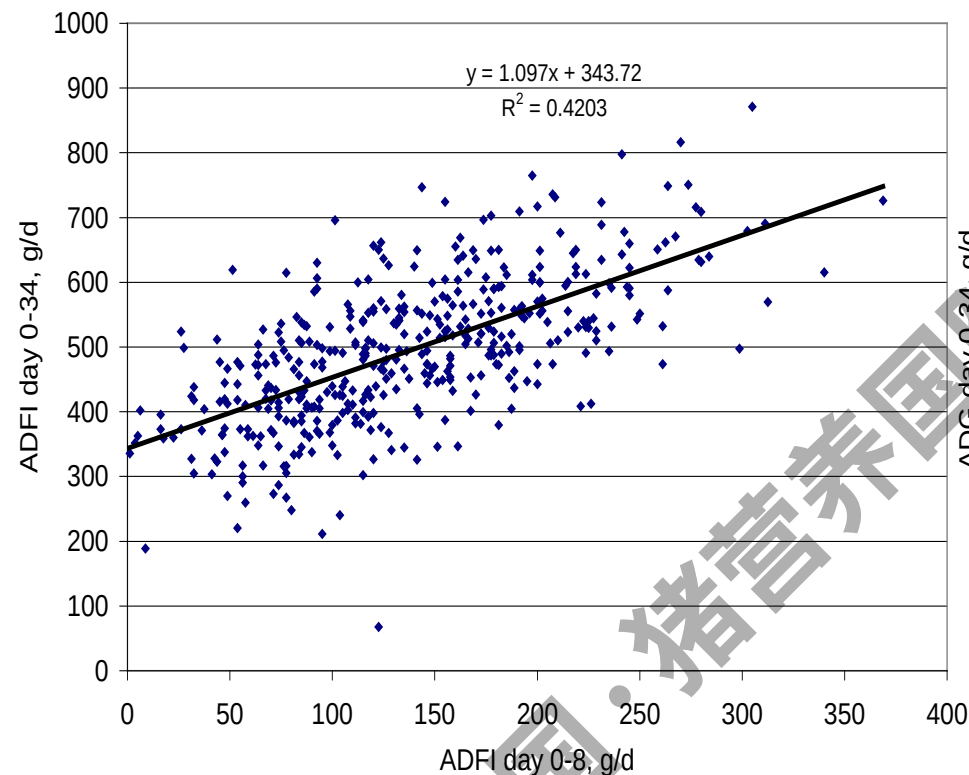
平均绒毛高度(μm)
Fed milk after weaning
断奶后饲喂奶



平均绒毛高度(μm)
Fed starter diet after weaning
断奶后饲喂教槽料

早期采食的重要性：实用性观点

The importance of early food intake: practical perspective



断奶后1周的采食量决定8 - 23kg 仔猪大约40%的采食量和增重

Food intake during wk 1 after weaning determines approximately 40% of food intake and gain between 8 - 23kg

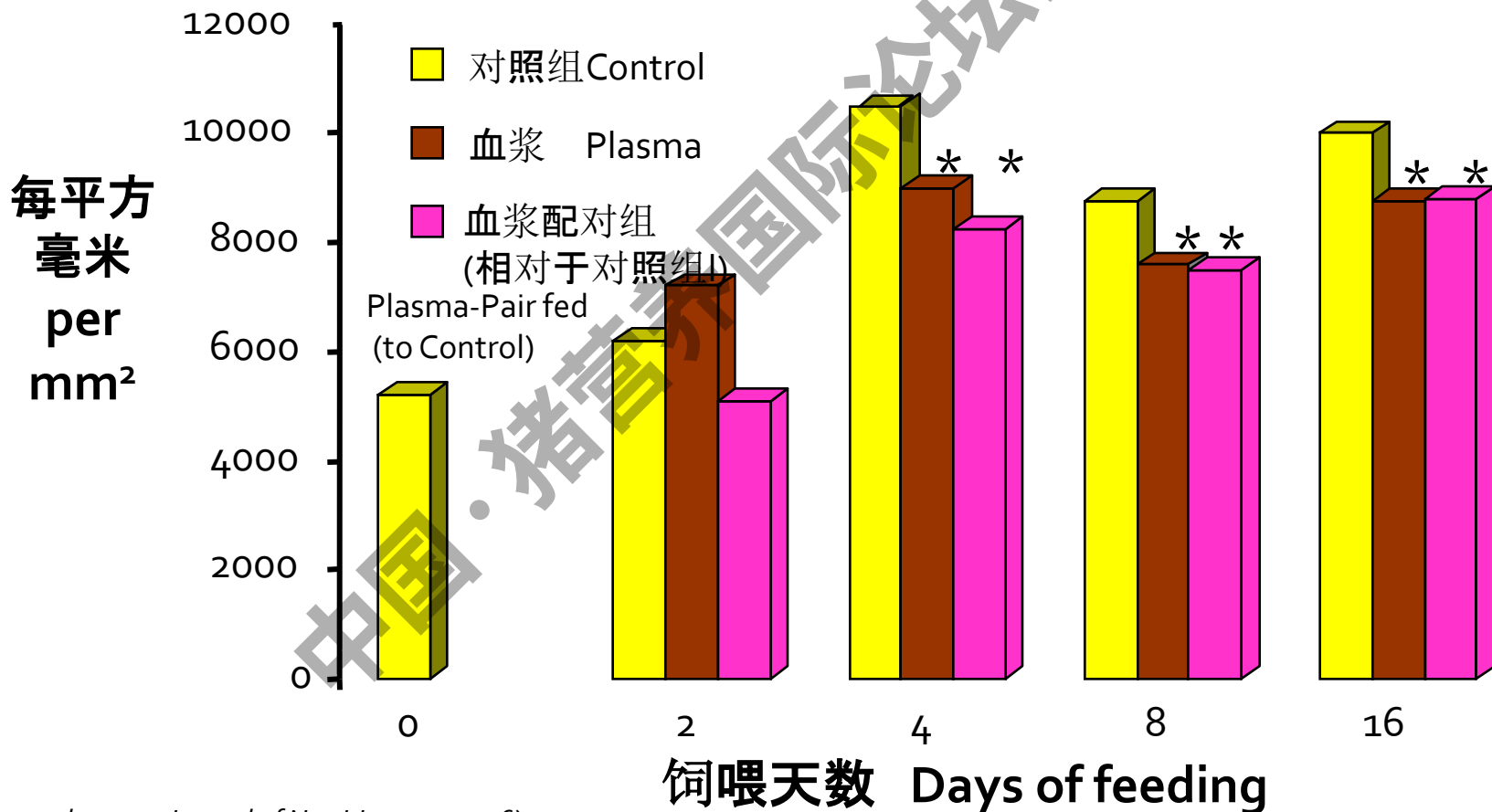
(Bruininx et al., 2004; *Journal of Animal Science* 79:301-308)

小结 Summary

- **断奶后上皮炎症影响小肠的渗透性和免疫功能**
Inflammation of epithelium after weaning influences permeability and immune function of the small intestine
- **这个机制，与肠道形态改变相关，主要是因为断奶后低采食量造成的** This mechanism, associated with changes in gut morphology, is linked to low feed intake after weaning
- **断奶后降低肠道炎症反应，** Reduce the inflammatory responses in the intestines after weaning,
 - 采食量最大化 Maximise feed intake
 - 减少应激(比如，降低减少促肾上腺皮质激素释放因子的产生和肥大细胞脱粒) Reduce stress (e.g., to reduce corticotropin releasing factor production and mast cell degranulation)
 - 研究能降低炎症和免疫功能的特异性饲料原料 Investigate specific feeding ingredients that could act to reduce inflammatory/immune responses

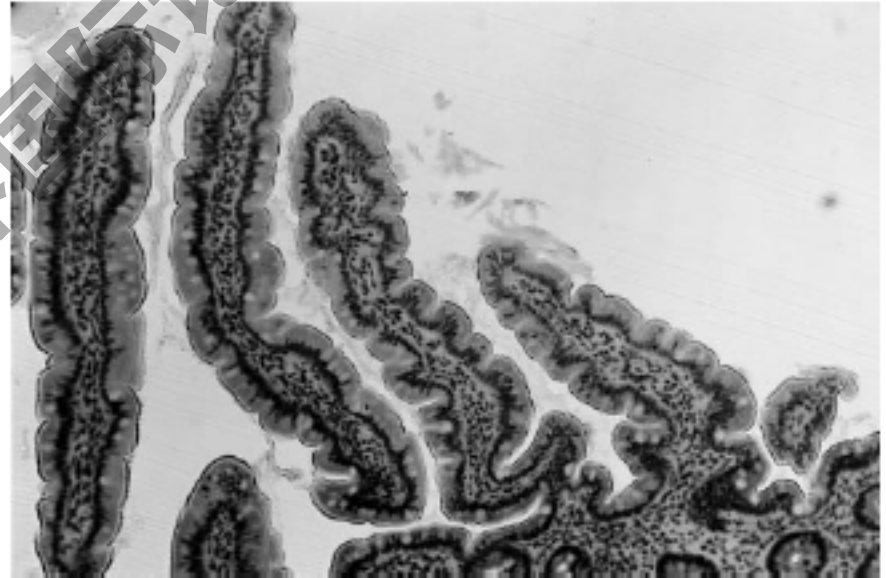
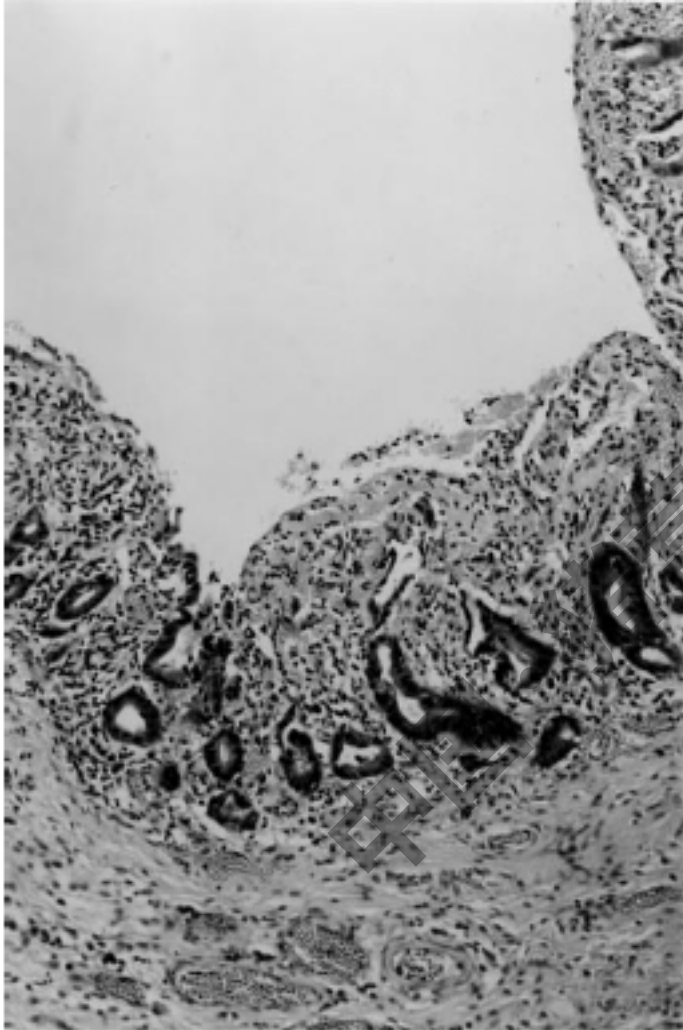
血浆能降低断奶仔猪空肠固有层细胞密度 以及减缓炎症反应

Feeding plasma reduces lamina propria cell density in the jejunum
and ameliorates the inflammatory response after weaning



患有坏死性肠炎的儿童在表皮生长因子注射之前(LHS)以及7天之后(RHS)的小肠切片

Small intestinal biopsies of a child with necrotizing enterocolitis before (LHS) and 7 days after (RHS) infusion of EGF



抗生素在畜牧业生产中的使用

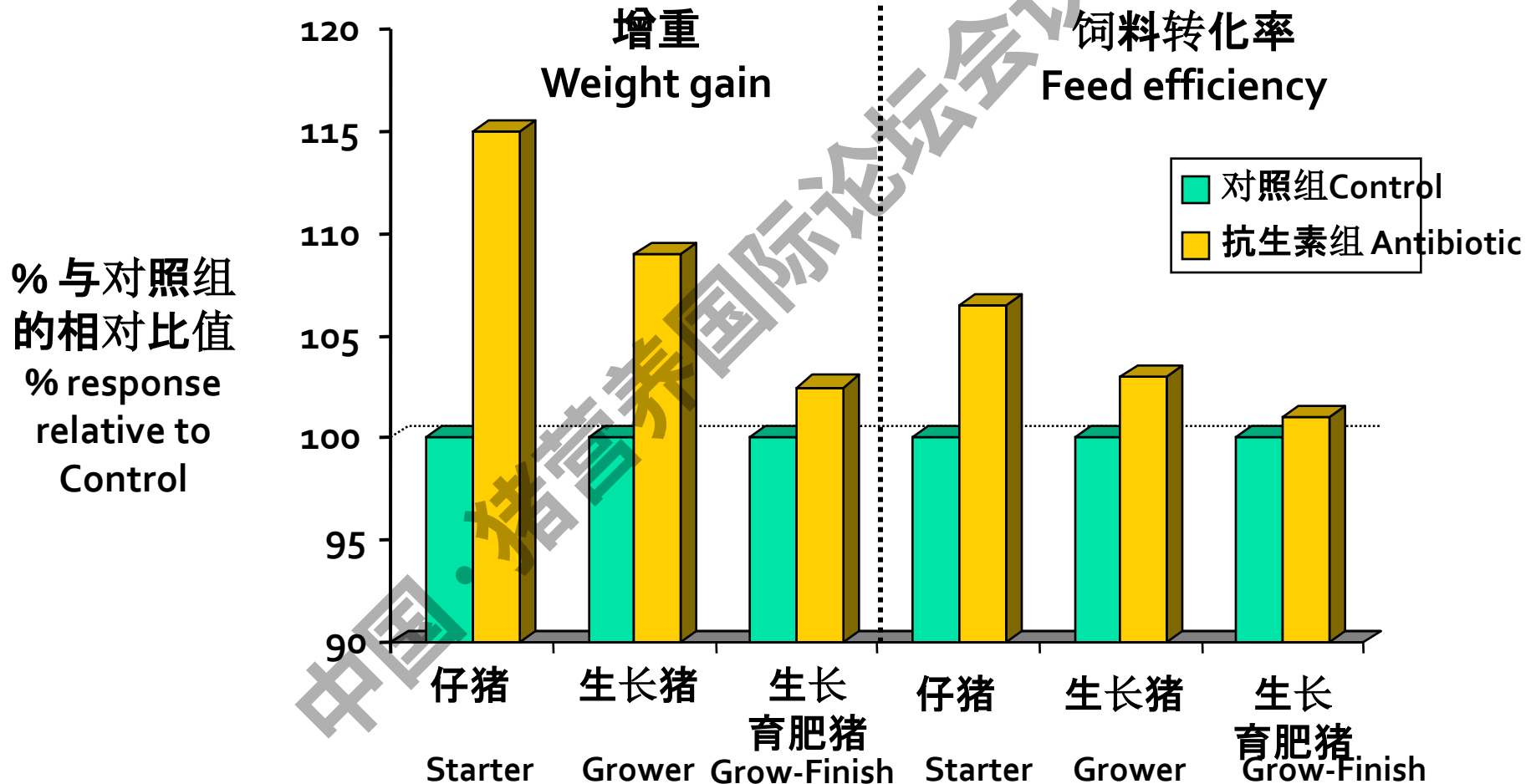
Antibiotic uses for the livestock industries

- **治疗** Therapeutic
 - 生病的动物 Sick animals
- **预防** Prophylaxis
 - 预防感染 Prevent infection
- **促生长** Growth promotion
 - 增重 Weight gain
 - 饲料转化率 Feed efficiency
 - 降低疾病发生率 Reduces disease incidence



抗生素促生长和生产性能(> 250 个研究结果)

Growth promoting antibiotics and performance (> 250 studies)



猪肉生产已发生了显著变化

But - Pork Production has Changed Dramatically



多点生产，年龄分群以及卫生防疫程序显著降低了慢性细菌性疾病的困扰
Multi site production, age segregation, and hygiene procedures have dramatically reduced the burden of chronic bacterial disease

**假设：饲料中添加抗生素引起的生产反应
在多点式生产体系中会降低。**

Hypothesis: Production response to in-feed antimicrobials should be reduced in multi-site pig production systems

现代化生产体系下，保育猪和生长育肥猪日粮中添加抗生素的效果

Effectiveness of in-feed antibiotics in nursery and grow-finish pigs reared in modern production systems*

在现代养殖模式下，抗生素在保育猪和生长育肥猪日粮中添加效果*

Table 2: Effectiveness of in-feed antibiotics in nursery and grow-finish pigs reared in modern production systems*		
参数	对照组	抗生素组
Parameter	Control	Antibiotic†
Nursery phase 保育阶段		
ADG (lb)	0.96†	1.01†
F:G	1.44	1.42
Grow-finish phase 生长育肥阶段		
ADG (lb)	1.72	1.72
F:G	2.90	2.90

* Adapted from Dritz et al, 2002.³ Data from five and four experiments, involving 3648 and 2660 pigs, for the nursery and grow-finish phases, respectively.

† ADG was greater (5.0% difference) in nursery pigs treated with antibiotics than in controls (ANOVA; $P < .05$)

ADG = average daily gain; F:G = feed-to-gain ratio.

* 文献来自Dritz et al, 2002. 数据来自保育和生长肥育阶段各自的5个和4个试验，涉及3648和2660头猪。

† 与对照组相比，抗生素组保育猪的ADG显著增加5%

ADG=平均日增重； F: G=料肉比

提供最佳胃肠道健康的抗生素替代物

Alternatives/replacements for optimum gastrointestinal health

- 对抗生素改善生产性能机制的理解有限， Limited understanding of mechanisms of action of growth promoting properties of antibiotics,
 - 非抗生素产品不可能拥有与抗生素完全相同的作用机制 Unlikely that non-antibiotic products will have exactly the same mechanisms
- 不同的条件 (动物, 饲料, 环境) 将最有可能引起不同的结果和需要不同的干预措施 (营养/管理) Different conditions (animal, feed, environment) will most likely cause different outcomes and require different interventions (nutritional / management)
- 很多同一类型产品，矛盾的/缺乏信息 Many 'types' of the same product; conflicting/lack of information
- 确定拥有广泛应用的最佳产品组合，需要付出大量的努力，例如，重复性、有效性以及昂贵的成本。 Identifying the optimum combinations of products that have wide application requires considerable effort, e.g., replication and validation, and is expensive

抗生素介导的通过对小肠菌群的影响而产生的影响

Proposed effects of antibiotics, mediated via effects on small intestinal microbiota

小肠微生物菌群抑制生长

Microbes in small intestine depress growth

抗生素能逆转微生物菌群对生长的抑制

Antibiotics reverse microbially-induced growth depression

直接 DIRECT

减少与宿主的营养竞争

Reduced competition
with host for nutrients

改善增重和饲料效率

**IMPROVED GROWTH AND
FEED EFFICIENCY**

间接 INDIRECT

降低生长抑制代谢物的产量, Decreased
production of growth-depressing metabolites,

- 芳香酚类 Aromatic phenols
- 氨 Ammonia
- 胆汁降解产物 Bile degradation products

减少肠黏膜的周转 Reduced turnover of gut mucosa

- 成熟的粘蛋白 Mature mucin
- 消化酶 Digestive enzymes
- 肠道形态学 (更薄的肠上皮)
Gut morphology (thinner epithelium)

最佳肠道健康的抗生素替代物

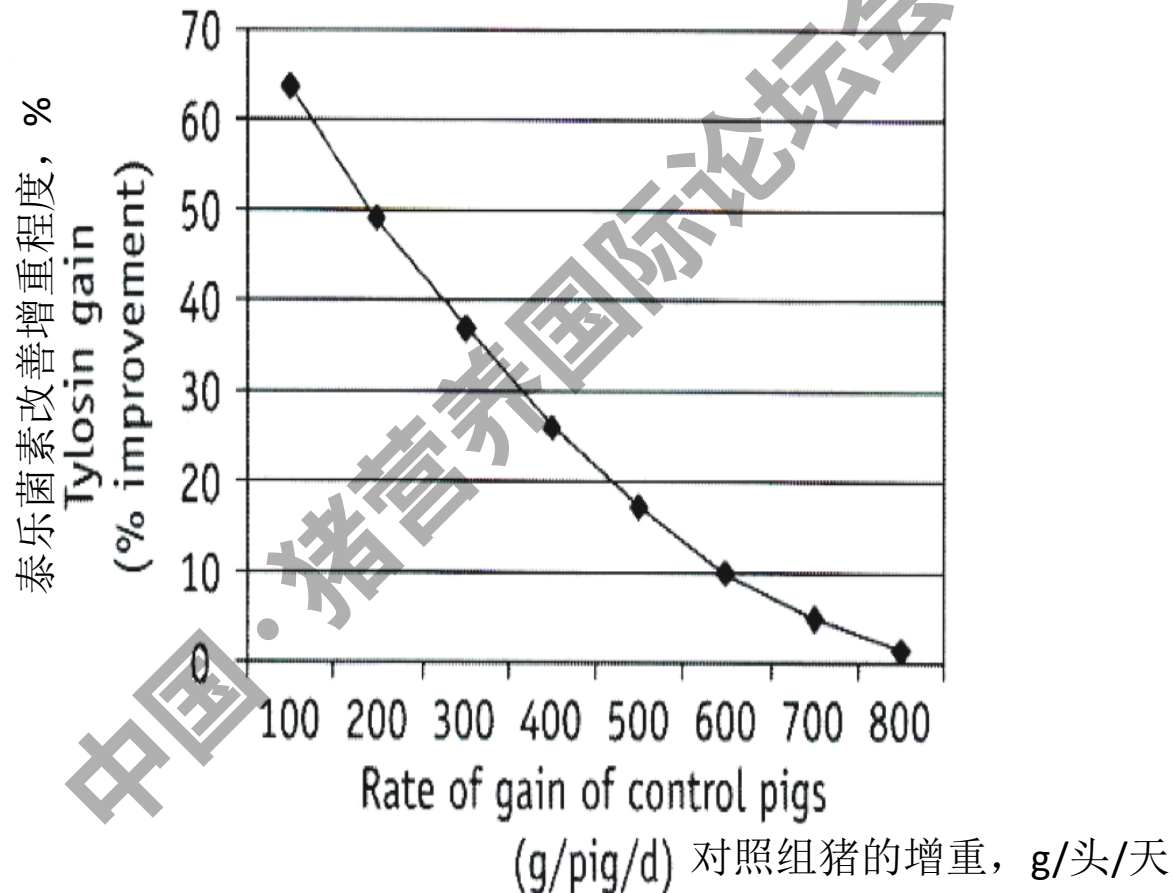
Alternatives/replacements for optimum gastrointestinal health

nanisms

- 很多同一类型产品，矛盾的/缺乏信息 Many 'types' of the same product; conflicting/lack of information
- 确定广泛应用的最佳产品组合，需要付出很大的努力，例如，重复性、有效性以及昂贵的成本。 Identifying the optimum combinations of products that have wide application requires considerable effort, e.g., replication and validation, and is expensive
- 不同的条件 (动物, 饲料, 健康, 环境) 将最可能会引起不同的结果和需要不同的干预措施 (营养/管理) Different conditions (animal, feed, health, environment) will most likely cause different outcomes and require different interventions (nutritional / management)

对照组猪的生产性能对饲料中添加泰乐菌素反应程度的影响

The impact of the performance of control animals on the magnitude of the response to tylosin in pigs



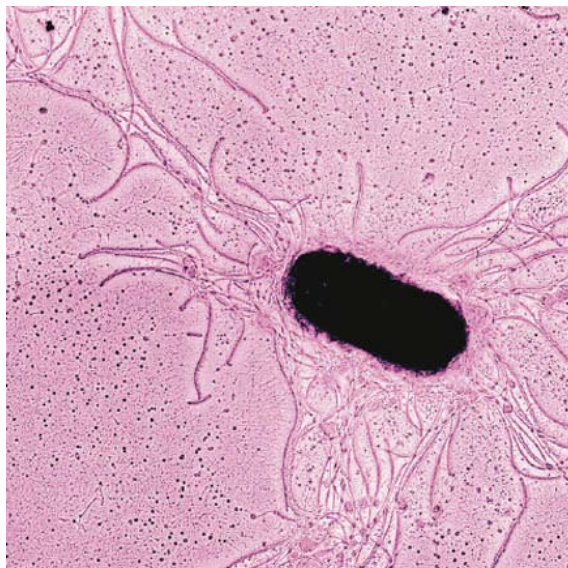
最佳胃肠道健康的抗生素 替代策略/方法

Some alternative strategies/approaches
for optimum gastrointestinal health

中国·猪营养网

大肠杆菌和断奶后大肠杆菌病(腹泻)

Escherichia coli and post-weaning colibacillosis (diarrhoea)



O 型血清型最可能与引起断奶后腹泻的 产肠毒素大肠杆菌相关

The O serogroups most frequently implicated as enterotoxigenic *E. coli* that cause post-weaning diarrhea

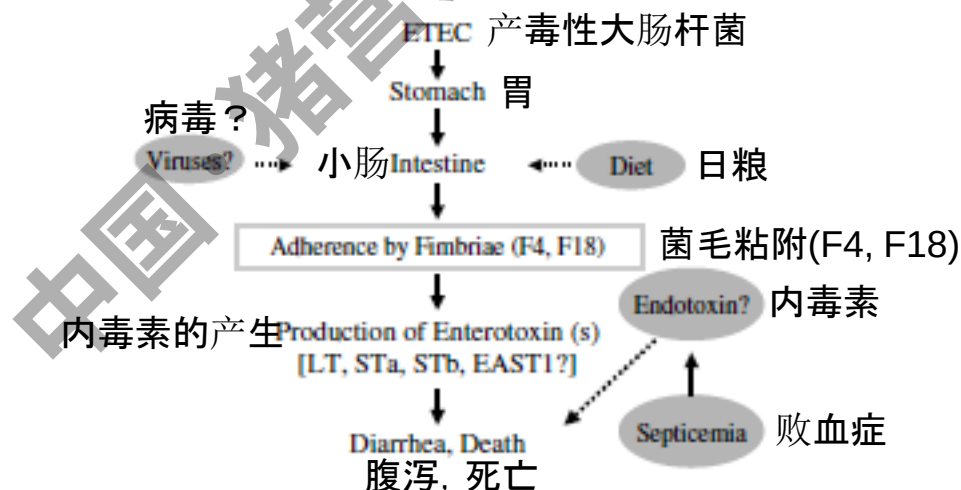
O 血清型 O serogroup	相关鞭毛抗原 Associated fimbrial antigens	H 相关抗原 Associated H antigens	作用 Comments
8	F4ab(K88ab), F4ac(K88ac)	H19	Less common than in earlier years
138	F18, F4ac*	H-, H4	Sometimes Stx2e+
139	F18	H1	Most commonly associated with ED
141	F18, F4ab, F4ac	H4	Sometimes Stx2e+
147	F4ac, F18	H6, H19	Sometimes Stx2e+
149	F4ac, F18*	H10, H19, H43, H-	Occasionally Stx2e+
157	F4ac	H19, H43	Occasionally Stx2e+

Sources: Nagy et al., 1990; Harel et al., 1991; Salajka et al., 1992; Francis, 2002; Frydendahl, 2002; Prager et al., 2004.

*Infrequently.

断奶仔猪大肠杆菌性腹泻发展步骤的研究综述

Overview of steps in development of *E. coli* post-weaning diarrhea in pigs



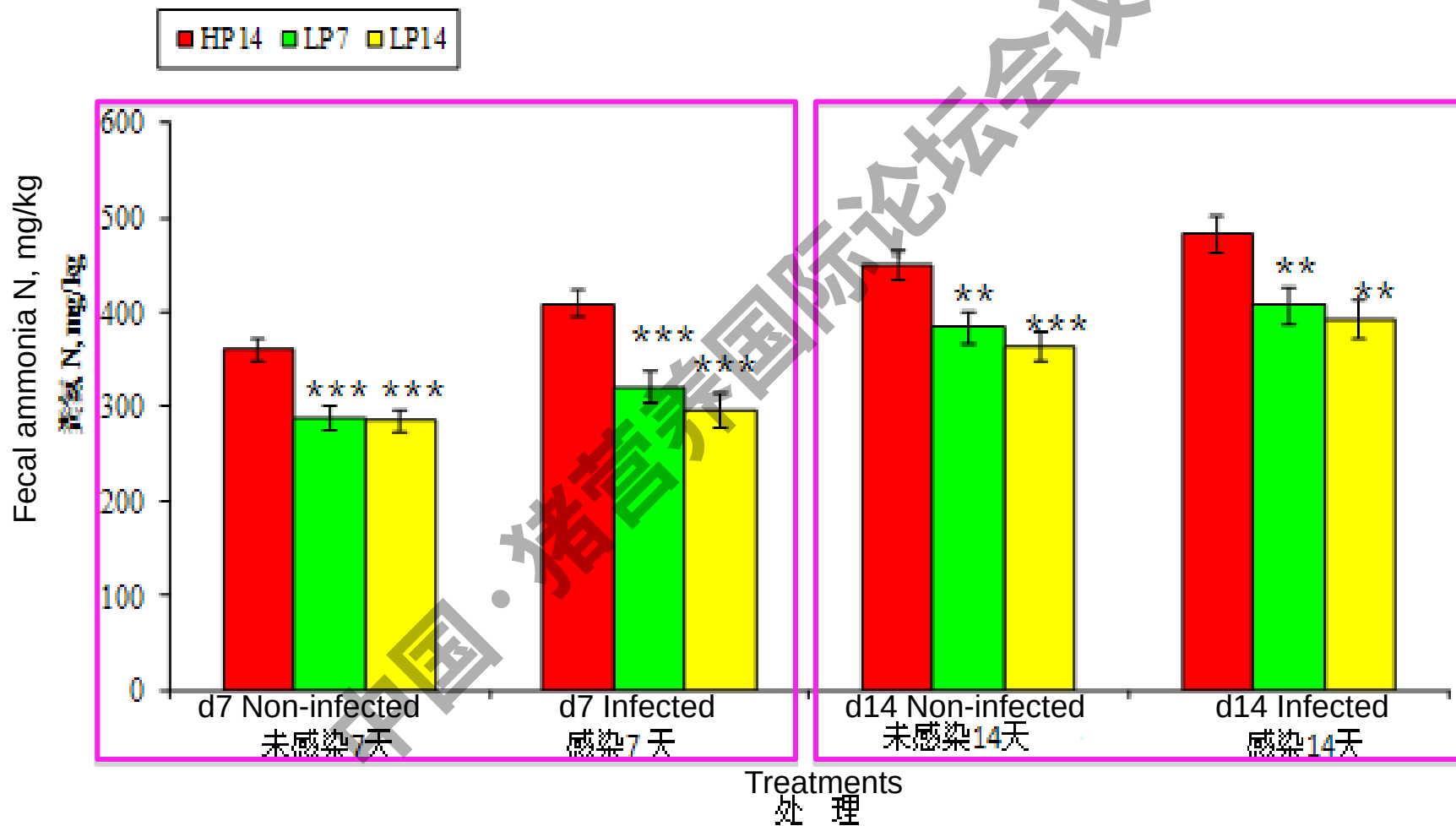
断奶仔猪饲喂低蛋白日粮减少腹泻

Feeding low protein diets to reduce scours after weaning

- 理论上讲:采食低蛋白日粮 (每kg断奶料蛋白含量< 180 g) 会降低腹泻, In theory: feeding low protein diets (< 180 g of protein per kg of weaner diet) should reduce diarrhea
- 然而 – 这个蛋白水平下很难配制 “平衡” 蛋白日粮, 除非添加昂贵的合成氨基酸。 However – difficult to make a ‘balanced’ diet at this amount of protein, unless you add expensive synthetic amino acids,
 - 商业化生产的缬氨酸和异亮氨酸 Commercial manufacture of valine and isoleucine
- 之前的研究: 当日粮配制不当时, 低蛋白日粮会减少断奶后腹泻, 但也会降低其生长。 Previous studies - low protein diets reduce scours but also reduce growth after weaning, when they are not formulated correctly

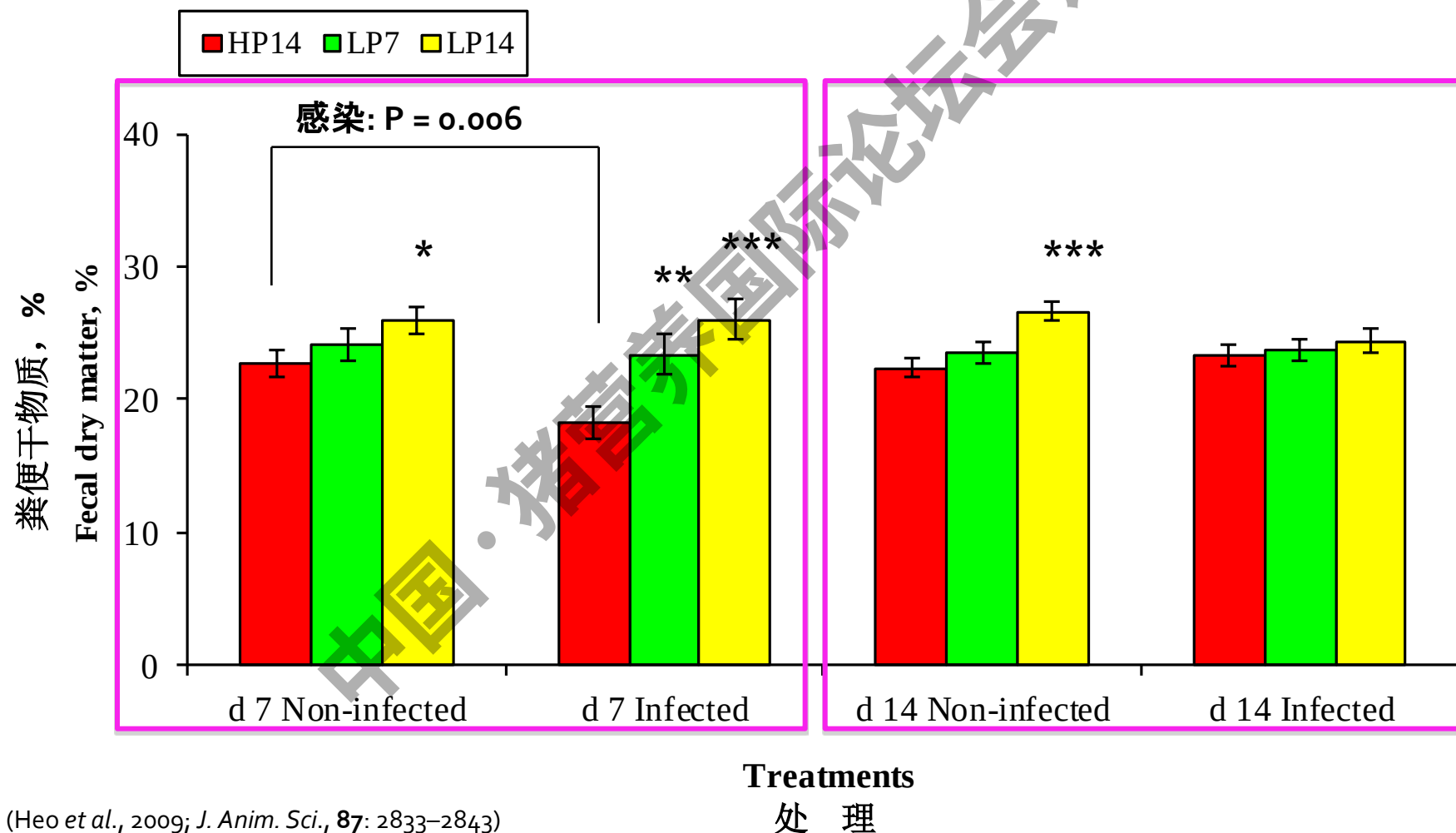
低蛋白日粮降低肠道氨的产量

Low protein diets reduce production of ammonia in gut



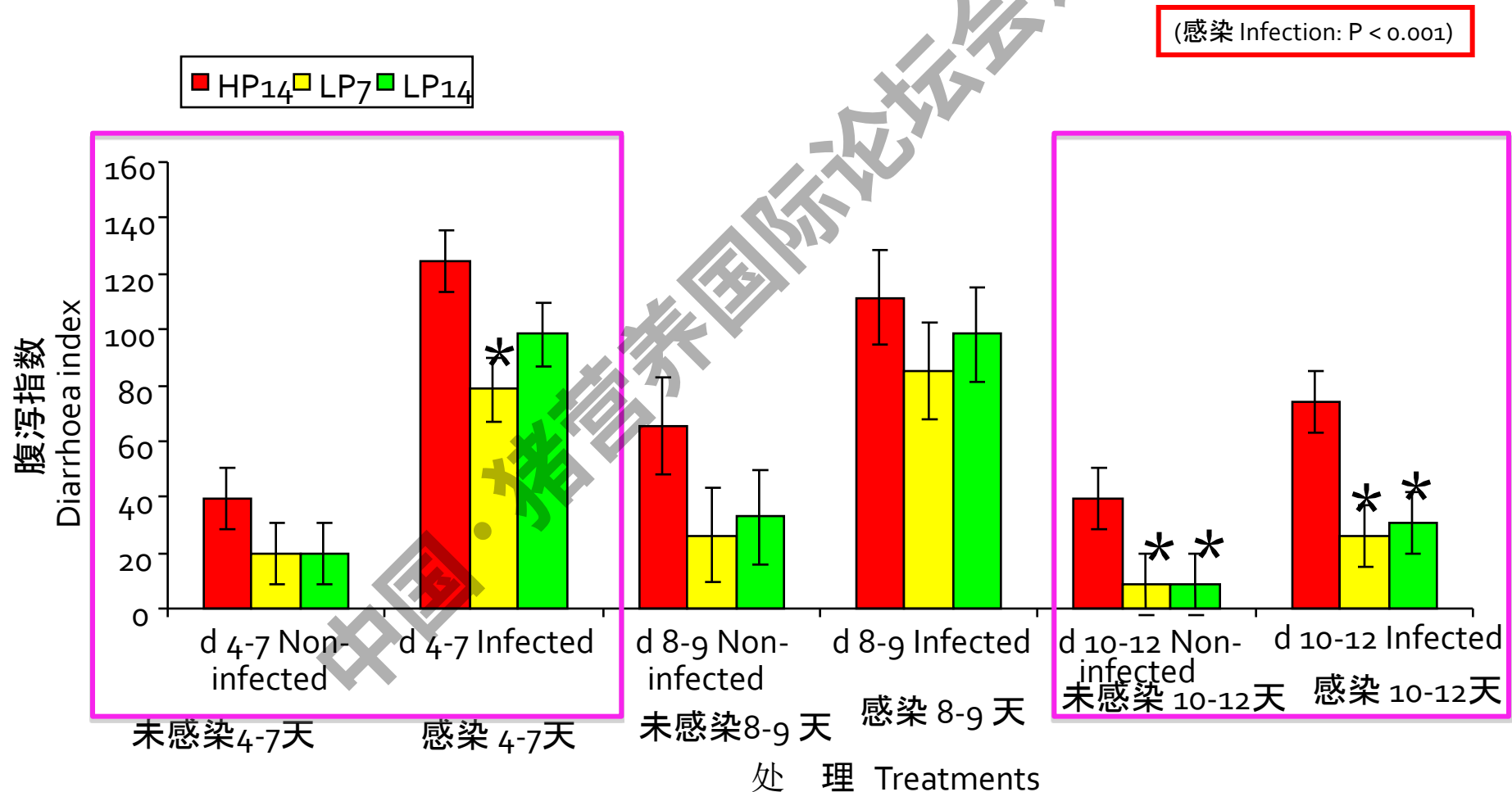
低蛋白日粮降低感染，但也增加粪便干物质含量，尤其在断奶后第一周

Infection decreases, and a low protein diet increases, dry matter content of faeces, especially in first week after weaning



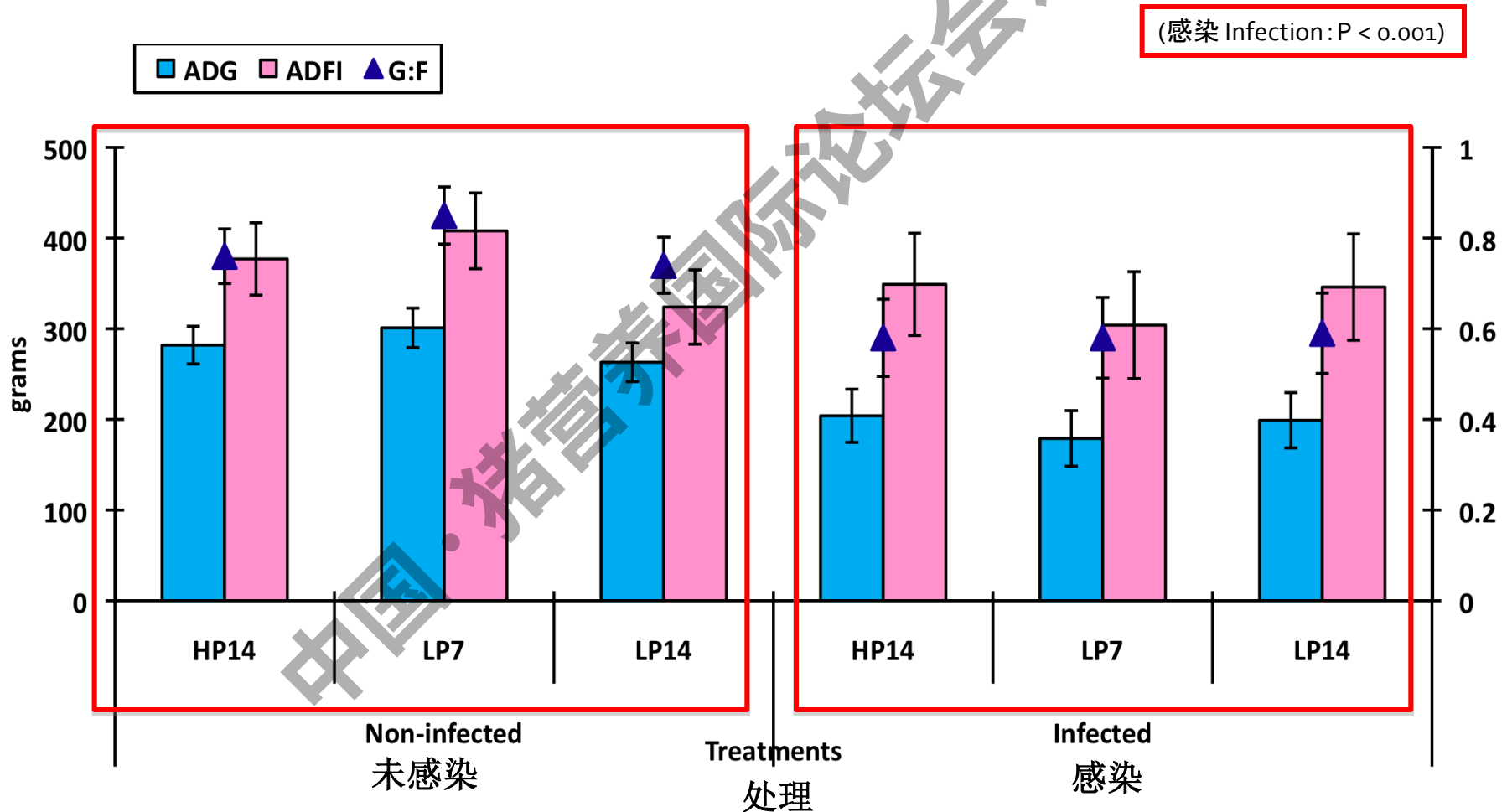
低蛋白日粮降低感染和未感染猪断奶后腹泻

Low protein diets reduce post-weaning diarrhoea in infected and non-infected pigs



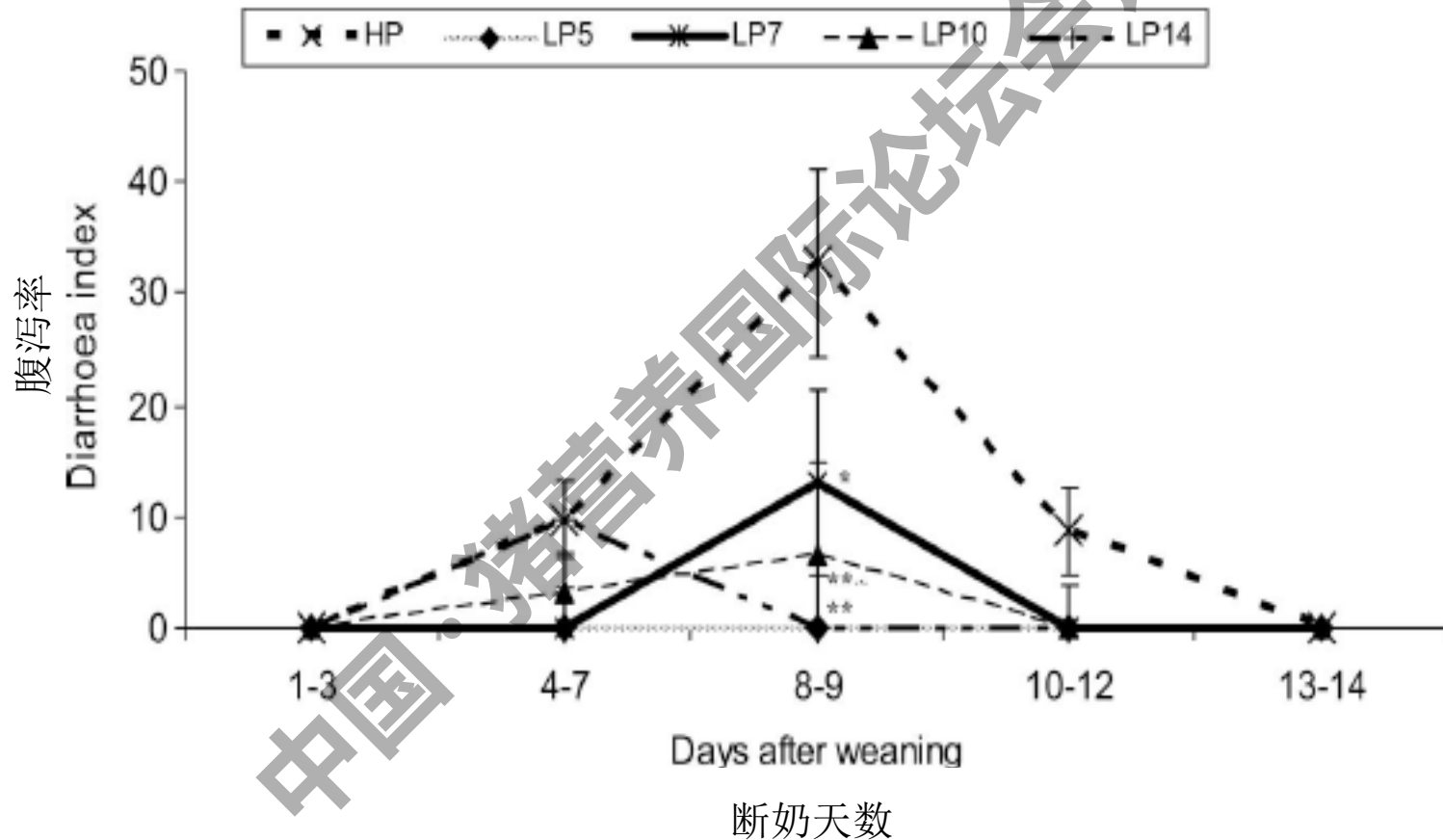
饲喂低蛋白日粮未降低生产性能

Feeding low protein diets does not decrease production



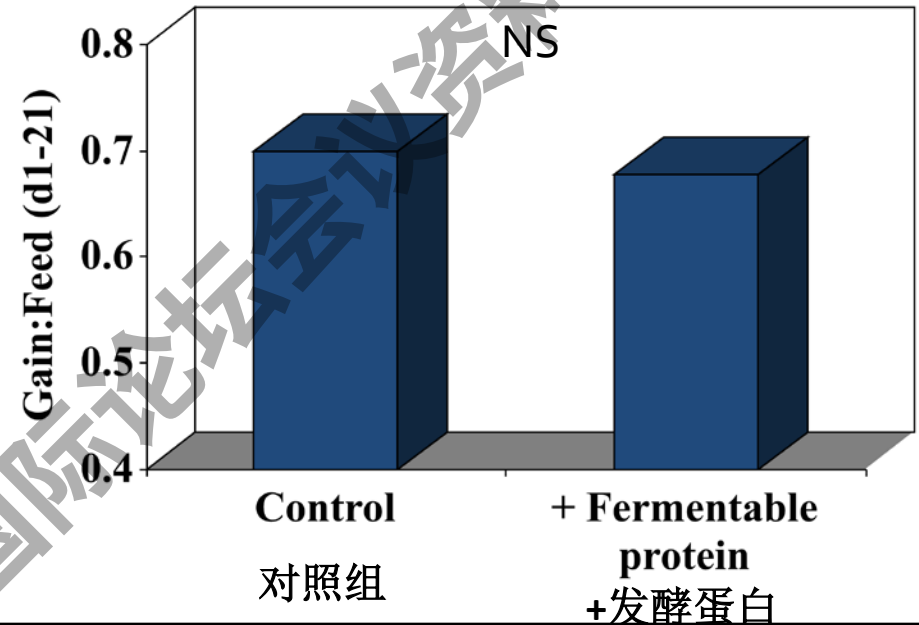
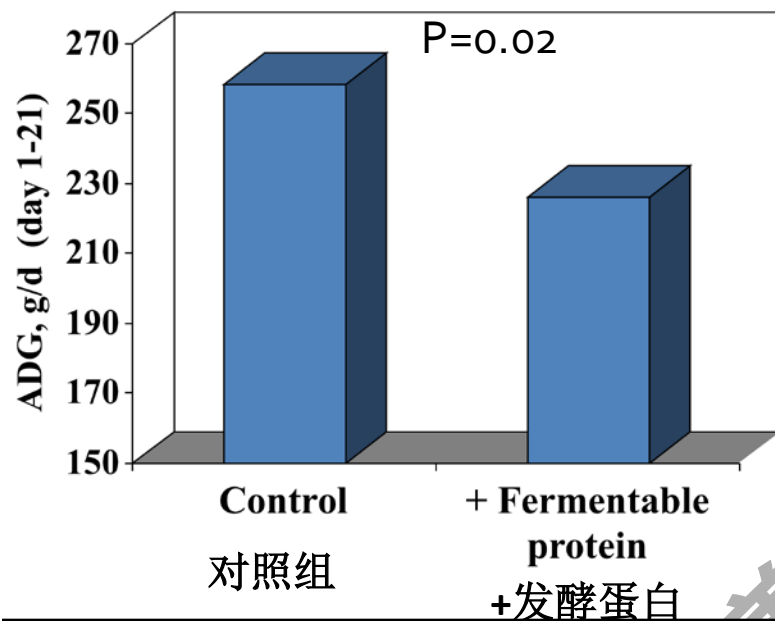
断奶后饲喂低蛋白日粮仅5天就能减少腹泻

Feeding a low protein diet for only 5 days post-weaning reduces diarrhea



发酵蛋白的负效应

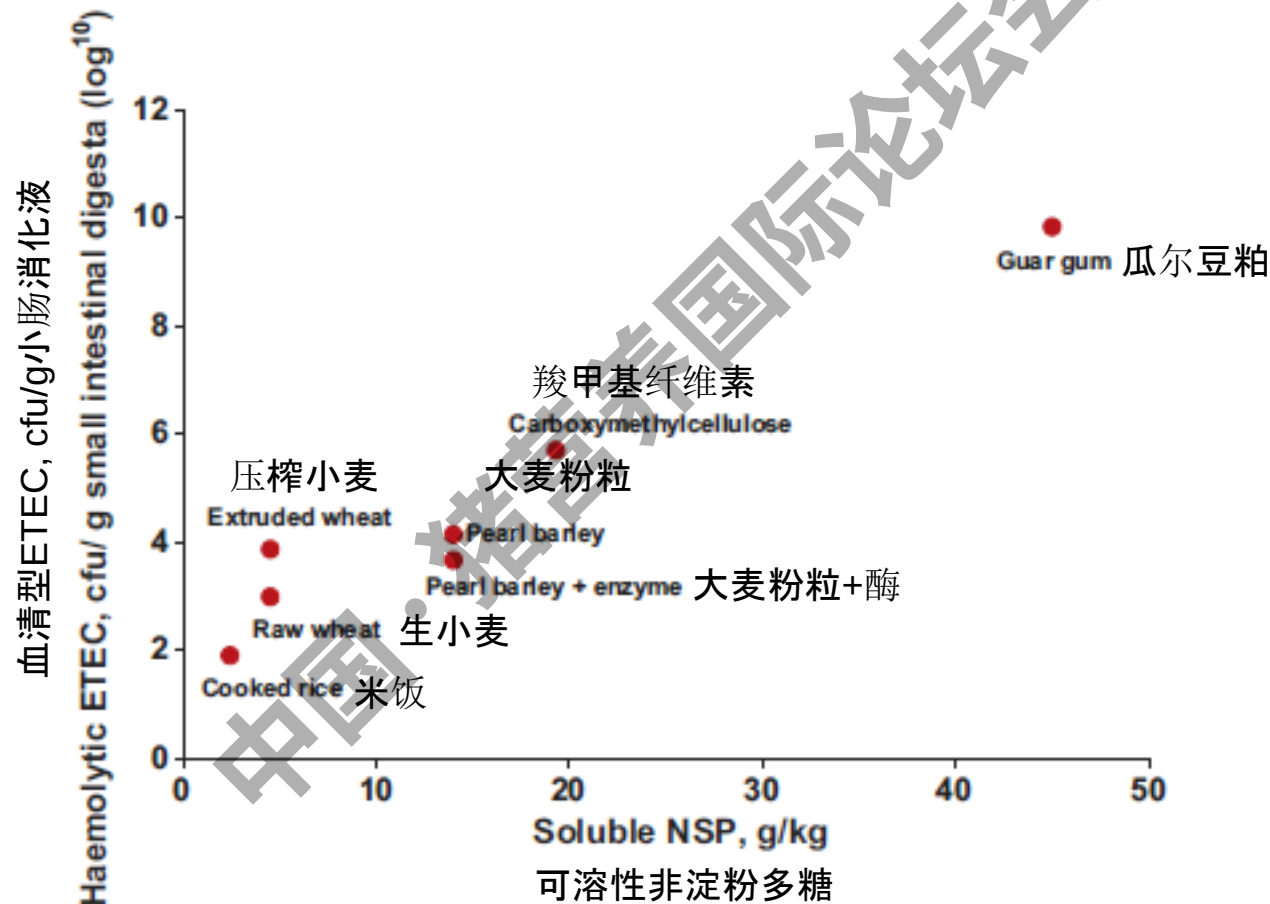
Negative effects of fermentable protein



	基础组	+ 发酵蛋白组	P值
	Control	+Fermentable protein	p-value
氮粪消化率 Fecal N digestibility, %	78.5	80.5	NS
氮回肠消化率 Ileal N digestibility, %	67.4	56.5	0.08
血尿氮, Blood urea N, mg/dl	6.5	9.5	<0.01
结肠梭状芽孢杆菌, Colon Clostridia, log cfu/ml	3.09	3.49	0.08

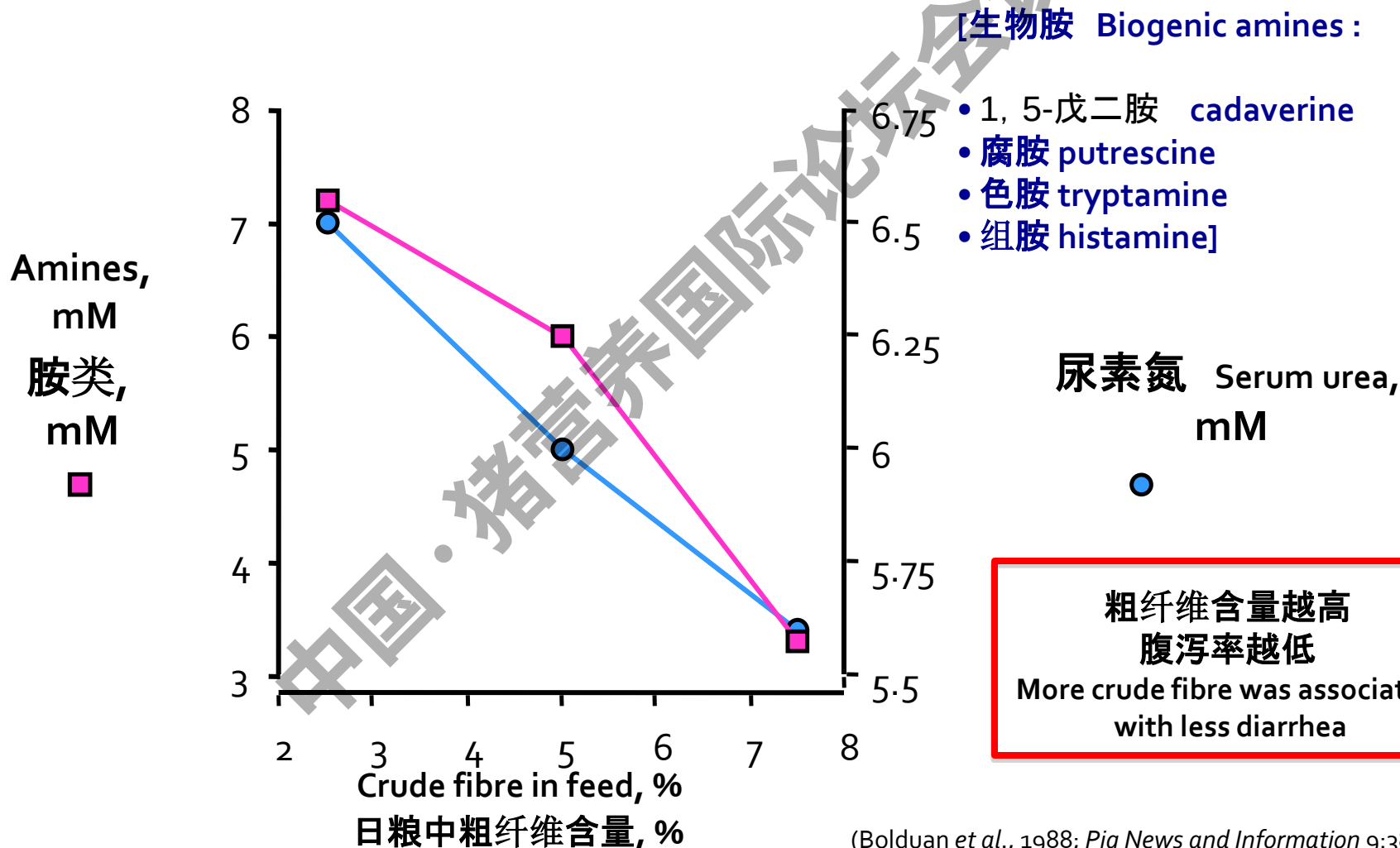
可溶性非淀粉多糖和通过肠道的溶血性大肠杆菌数量的关系

Relationship between soluble non-starch polysaccharides and viable small intestinal count of hemolytic ETEC



较高的非消化性纤维含量降低菌群氮的代谢

A higher indigestible fibre content reduces bacterial nitrogen metabolism



不可溶纤维和断奶后的大肠杆菌感染

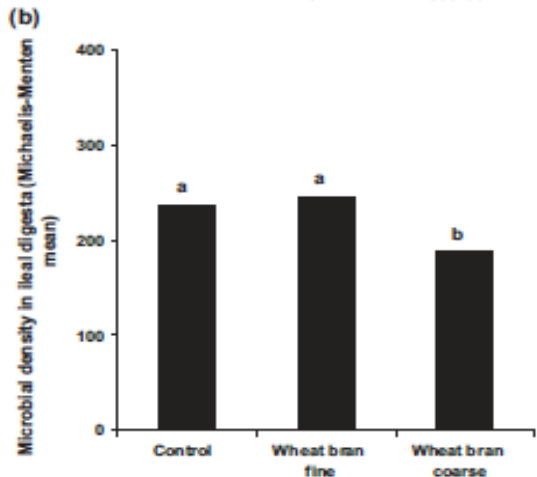
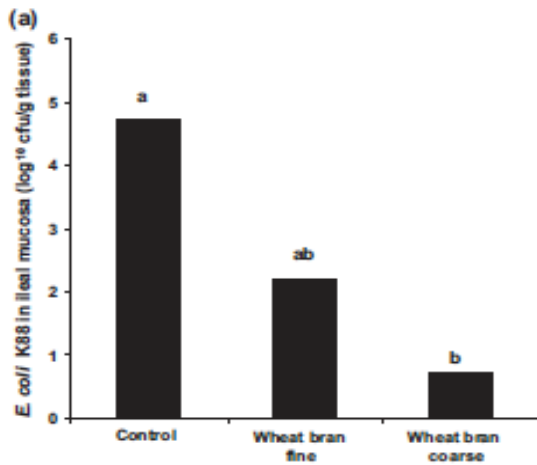
Insoluble fibre and *Escherichia coli* infection after weaning

断奶仔猪日粮中添加粗制小麦麸
(4%; 颗粒大小为1088 m)

降低了大肠杆菌 K88 感染率，

Inclusion of coarsely prepared wheat bran
(4%, particle size 1088 m) in a diet for weaner
pigs challenged with *E. coli* K88 decreased:

- (a) 回肠粘膜绑定大肠杆菌K88
ileal mucosa-bound *E. coli* K88;
- (b) 回肠食糜中菌群密度;
microbial density in the ileal digesta;
- (c) 粪样中戊酸的含量
proportion of valeric acid in faecal samples

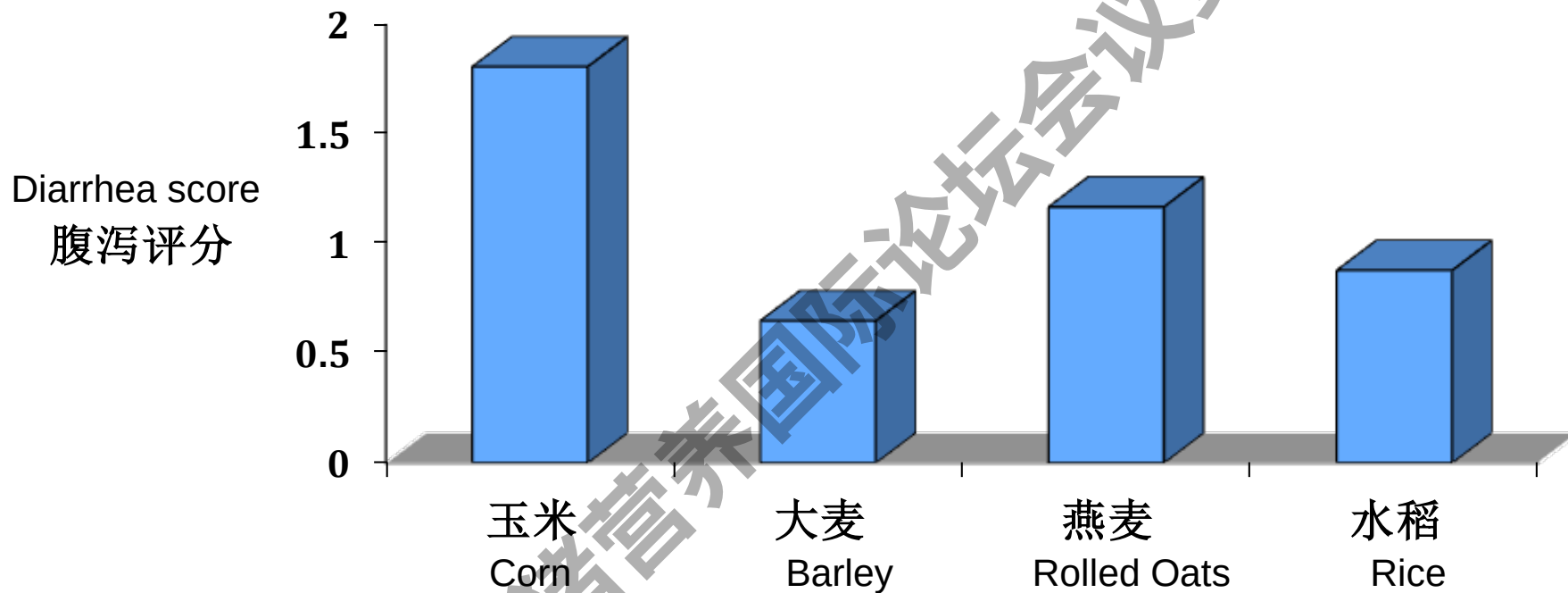


断奶仔猪饲喂不同谷物日粮对腹泻的影响

Pigs fed different cereals vary in diarrhea after weaning

$P < 0.01$

SE 0.22



猪口服 2×10^9 CFU/头的大肠杆菌感染；每个处理组6头21日龄断奶仔猪；腹泻评分 0= 正常粪便；4 = 严重腹泻 Pigs challenged with oral dose of 2×10^9 CFU/pig; 6 pigs weaned at 21 d of age / treatment; Diarrhea score 0= normal feces; 4 = severe (Buckingham *et al.*, 2006)

另外: 大麦日粮与和玉米日粮相比，减少了保育舍仔猪的移除：3.6 和 7.1% ($P < 0.05$) Also: reduced removal of pigs from nursery for barley vs corn: 3.6 vs 7.1% ($P < 0.05$) (Perez-Mendoza *et al.*, 2006)

饲料加工工艺影响病原菌的存活

Feed processing influences survival of pathogenic bacteria

- 胃: 作为致病菌进入肠道和在粪便中排出的一个屏障。 Stomach: can act as a *barrier* to pathogenic bacteria moving into intestines and passing out in feces

- Mikkelsen *et al.* (2004):

- 饲料颗粒大小(精细的 vs 粗糙的)
Feed particle size (fine vs coarse)
- 饲料形态(颗粒 vs 非颗粒) Feed form
(pelleted vs non-pelleted)



(<http://www.picsearch.com/pictures/science/bacteria%20om/salmonella%20bacteria.html>)

- 评估了菌群数量、饲料特性和血清DT12鼠伤寒沙门氏菌的存活
Assessed microbial populations, properties of feed, survival of *Salmonella enterica* Typhimurium DT12

约55 kg猪胃的特性

Stomach characteristics in pigs killed at ~ 55 kg

日粮类型

	精细-不制粒 Fine-Non-pelleted	精细-制粒 Fine-Pelleted	粗糙-不制粒 Coarse-Non-pelleted	粗糙-制粒 Coarse-Pelleted
DT ₁₂ 死亡率 DT ₁₂ death rate(/hr)	0.3	0.4	1.9	0.2
pH	4.3	4.3	3.9	4.7
有机酸 Organic acids,mM	5.3	3.3	26.5	6.2
结合型乳酸, Undissociated lactic acid , mM	0.9	0.8	10.2	1.7
乳酸菌 Lactobacillus, log ₁₀ CFU/g	6.8	7.0	7.9	7.4



益生菌/益生元作为抗生素替代 物的饲喂策略

Prebiotics/prebiotics as an alternative
feed strategy

益生菌，益生元和合生素

Probiotics, prebiotics and synbiotics

- **益生菌** – “对生命有利” -是一种功能性食物，被FAO和WHO定义为单一的或混合的生物，是活的微生物，当被饲喂足够数量时有利于宿主健康。 **Probiotic** – ‘for/in favor of life’ - is a functional food defined by the FAO/ WHO as mono or mixed cultures of ‘live microorganisms which, when administered in adequate amounts confer a health benefit on the host’
- **益生元**是在某些植物中被发现的一种纤维，不被消化可到达结肠，被FAO和WHO定义为“不被消化的物质，通过选择性的刺激肠道少量固有菌的增殖和活性，给宿主提供一个有益的生理效应”。 A **prebiotic** is a fiber found in some plants that reaches the colon undigested, and were defined by the FAO/ WHO as ‘nondigestible substances that provide a beneficial physiological effect on the host by selectively stimulating the favorable growth or activity of a limited number of indigenous bacteria’
 - **Gibson *et al.* (2010):** “一种选择性发酵成分能引起肠道菌群组成和活性的变化，这种变化对健康有益。” Gibson *et al.* (2010): ‘a selectively fermented ingredient that causes specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health’
- **合生素** 是一些营养性补充剂，为一些益生菌和益生元的组合 **Synbiotics** are nutritional supplements that are combinations of probiotic bacteria and prebiotic food ingredients,
 - 声称能够改善益生菌的生存能力和传递特异的健康功效（神人协力合作说）。 Claimed to improve the viability of probiotics and to deliver specific health benefits (synergism)

乳酸杆菌属和双歧杆菌属的益生菌，益生素和合生素

Examples of probiotics, prebiotics and synbiotics using
Lactobacillus and *Bifidobacteria* spp.

	Probiotic	Prebiotic	Synbiotic
<i>Lactobacillus</i> sps.	<i>L. acidophilus</i> 嗜酸乳杆菌	Fructo-oligosaccharides 果寡糖	Lactobacilli + lactitol 乳酸菌+乳糖醇
乳酸菌属	<i>L. amylovorus</i> 淀粉乳杆菌	(FOS) 低聚果糖	Lactobacilli+ inulin 乳酸菌+菊粉
	<i>L. bulgaricus</i> 保加利亚乳杆菌	Inulin 菊粉	Lactobacilli + FOS or 菊粉
	<i>L. brevis</i> 短乳杆菌	Lactulose 乳果糖	inulin 乳酸菌鼠李糖
	<i>L. casei</i> 干酪乳杆菌	Lactitol 乳糖醇	Lactobacillus rhamnosus
	<i>L. cellobiosus</i> 纤维二糖乳杆菌	Galactooligosaccharides (GOS) 低聚半乳糖	GG + inulin GG+菊粉
	<i>L. crispatus</i> 卷曲乳杆菌	Isomaltooligosaccharides 异麦芽低聚糖	Bifidobacteria + FOS
	<i>L. curvatus</i> 弓形乳杆菌	Xylooligosaccharides 低聚木糖	Bifidobacteria + GOS
	<i>L. fermentum</i> 发酵乳杆菌	Lactosucrose, 低聚乳果糖	Bifidobacteria and
	<i>L. gallinarum</i> 鸡乳杆菌	Cereals fibres 谷物纤维	Lactobacilli + FOS
	<i>L. johnsonii</i> 约氏乳杆菌		or inulin
	<i>L. lactis</i> 乳酸乳杆菌		
	<i>L. paracasei</i> 副干酪乳杆菌		
	<i>L. plantarum</i> 植物乳杆菌		
	<i>L. salivarius</i> 唾液乳杆菌		
	<i>L. sporogenes</i> 芽孢乳杆菌	Soy oligosaccharides 大豆低聚糖	
	<i>L. reuteri</i> 罗伊氏乳杆菌	Raffinose 棉籽糖	
	<i>L. rhamnosus</i> 鼠李糖乳杆菌		

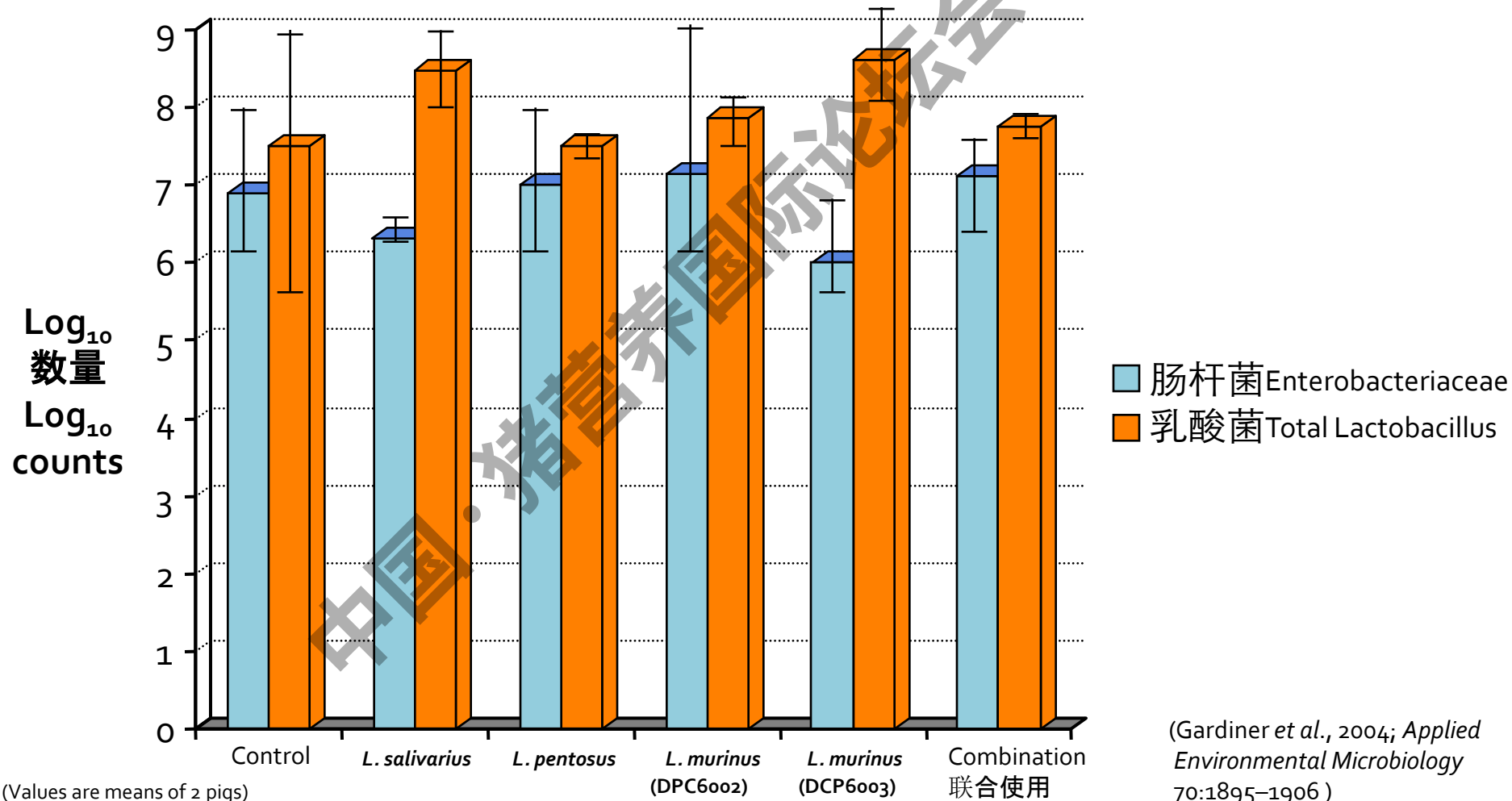
口服乳酸杆菌添加剂对断奶仔猪的作用

Effects of orally administered *Lactobacillus* spp. in weaned piglets

- Gardiner *et al.* (2004),
 - 获得从猪的盲肠内容物中分离的各种乳酸杆菌 Obtained various *Lactobacillus* isolates from pig caecal contents
- 口服后测定断奶仔猪肠道内的菌群存活/存留量，以及减少肠杆菌（沙门氏菌，大肠杆菌）数量的能力。 Measured survival and persistence in gut of weaner pigs after dosing, and ability to reduce *Enterobacteriaceae* (*Salmonella*, *E. coli*) counts
- 研究发现，在存活/存留量和降低肠杆菌数量上，不同菌株间存在巨大不同。 Found large differences in strains used, both in survival/persistence and in their ability to reduce *Enterobacteriaceae* counts

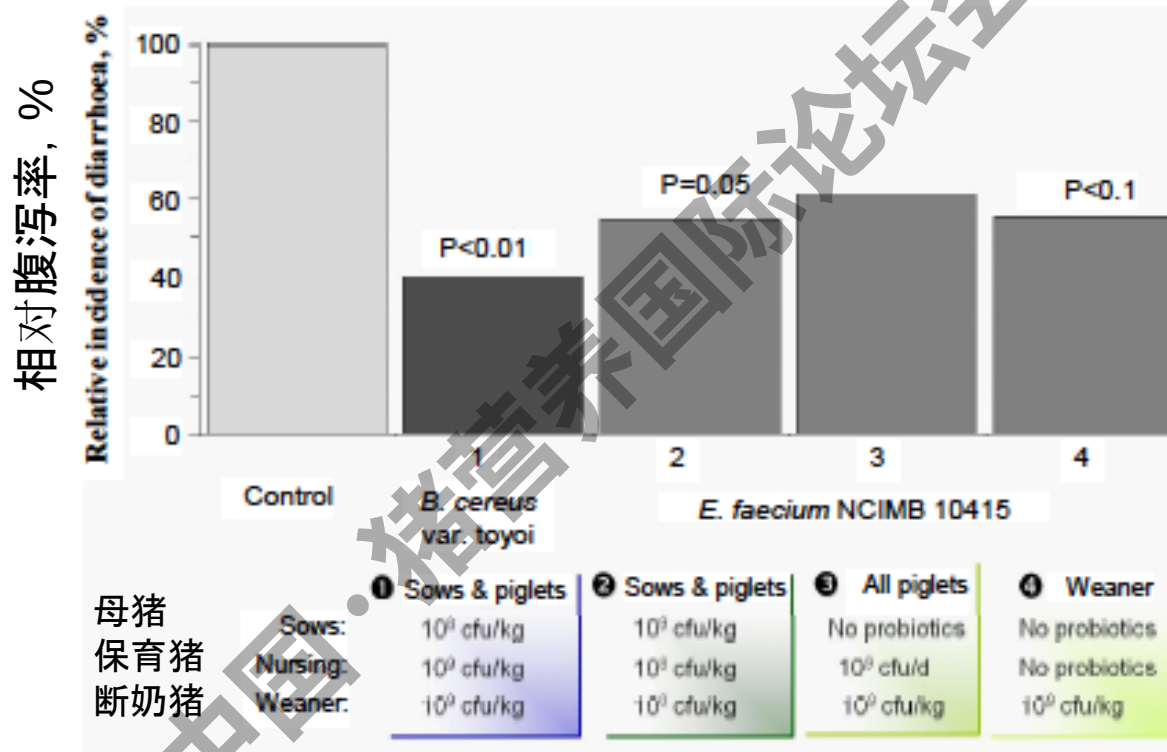
口服益生菌9天后的小猪盲肠内容物中肠杆菌和总乳酸菌的数量

Enterobacteriaceae and total *Lactobacillus* counts in caecal contents ($\pm$ s.d.) of young pigs 9 days after oral dosing



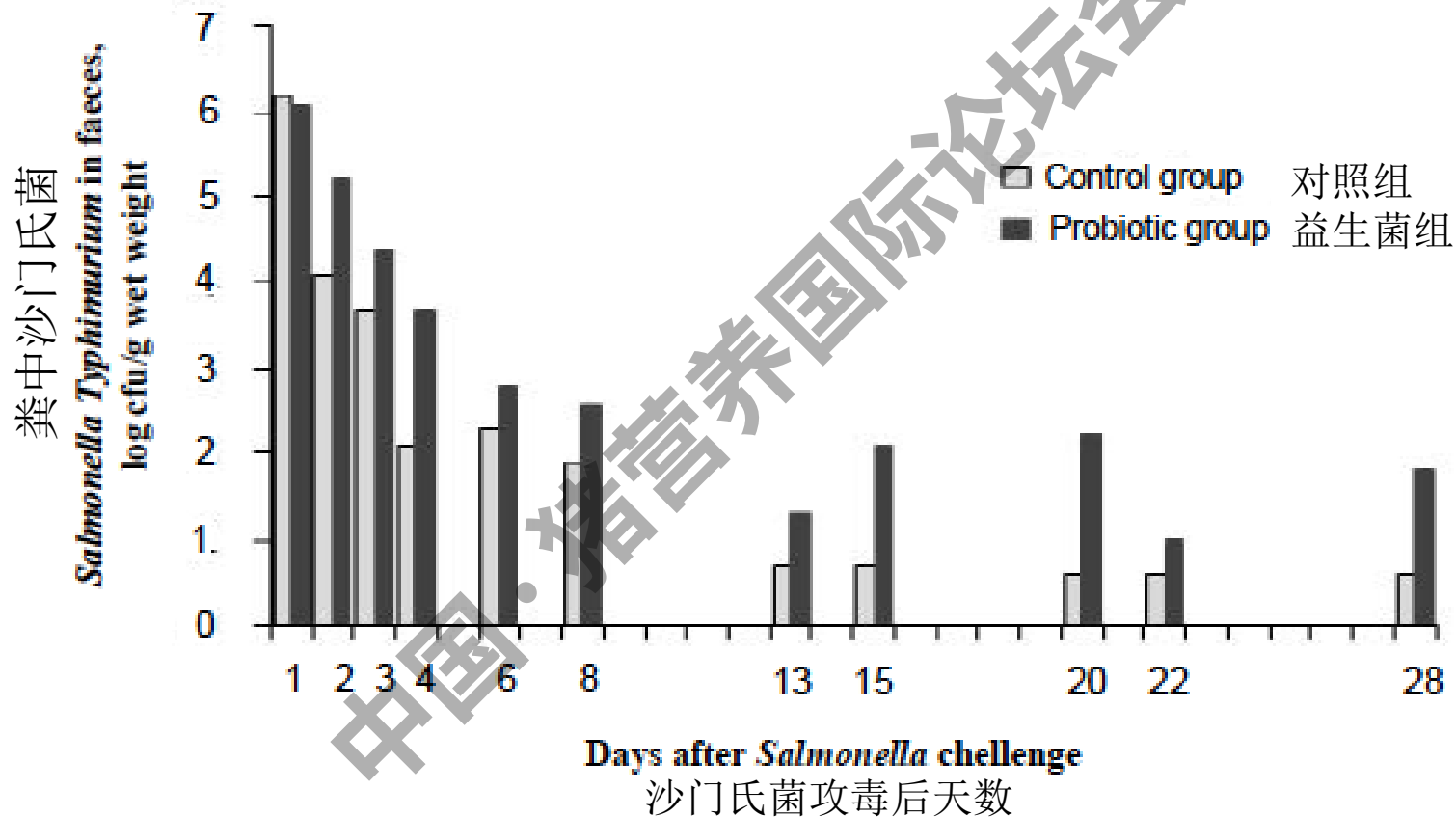
屎肠球菌NCIMB 10415 和蜡样芽孢杆菌降低腹泻 (设置对照组发病率为100%)

Enterococcus faecium NCIMB 10415 and *Bacillus cereus* var. *toyoi* reduce diarrhoea (incidence in control animals set at 100%)



给猪饲喂屎肠球菌然后口服沙门氏菌攻毒 增加了猪粪中沙门氏菌的排出量

Faecal excretion of *Salmonella* was increased in pigs fed *E. faecium* following oral challenge





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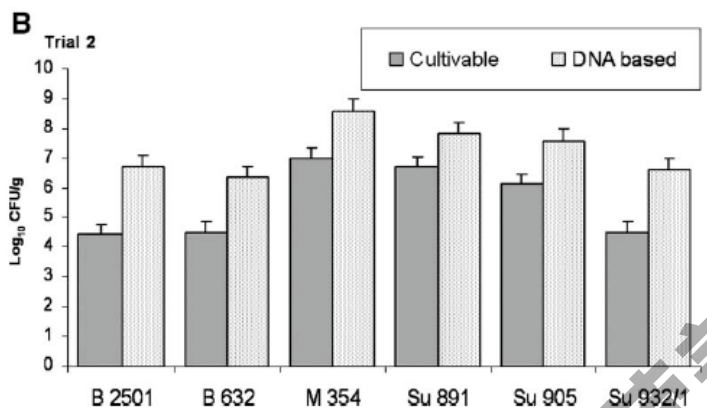
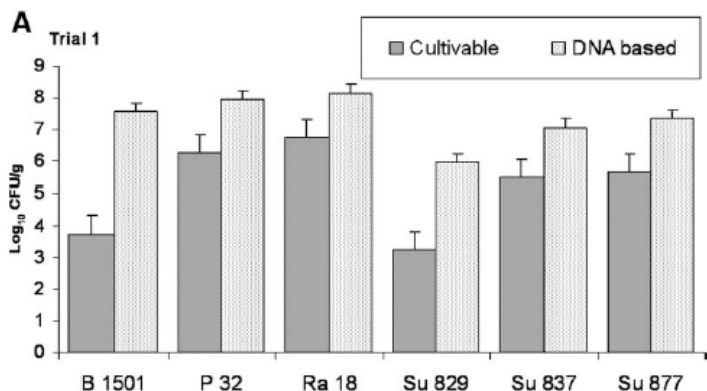
A novel strategy to select *Bifidobacterium* strains and prebiotics as natural growth promoters in newly weaned pigs

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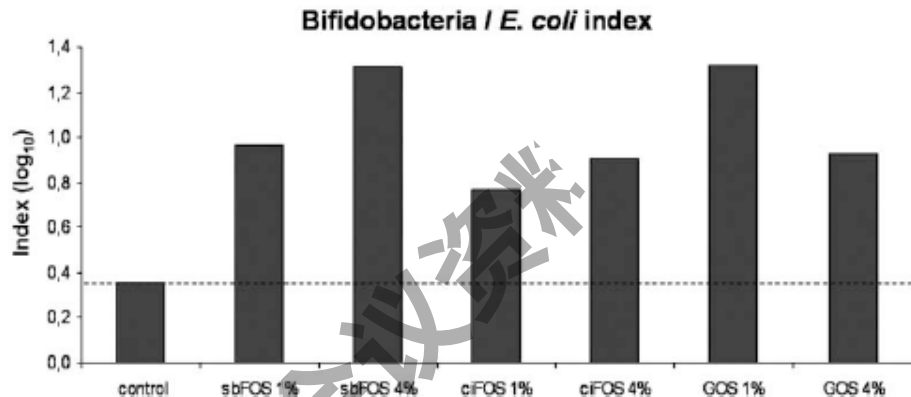
- 评估不同双歧杆菌属添加剂与不同益生元组合物的联用[FOS(甜菜碱), 菊粉, GOS (奶粉)]对胃肠道中双歧杆菌属添加剂存活量的影响
Evaluated different strains of *Bifidobacterium* spp., in combination with different prebiotic combinations [FOS (from sugar beet), inulin, GOS (from milk whey)], for survival of *Bifidobacterium* spp. in the gastrointestinal tract
- 评估最佳益生菌菌属的不同日添加剂量的影响
Evaluated different daily doses of the most promising probiotic strains
- 研究发现, 每头猪每天饲喂 10^{11} CFU的*B. animalis* subsp. *lactis* Ra 18, 是提高生产性能最好的益生菌选择。
Found that *B. animalis* subsp. *lactis* Ra 18, at 10^{11} CFU per pig per day, was the best probiotic choice for improved performance



用平板计数和直接半定量PCR的方法，研究不同双歧杆菌菌株对盲肠内容物中双歧杆菌数量的影响

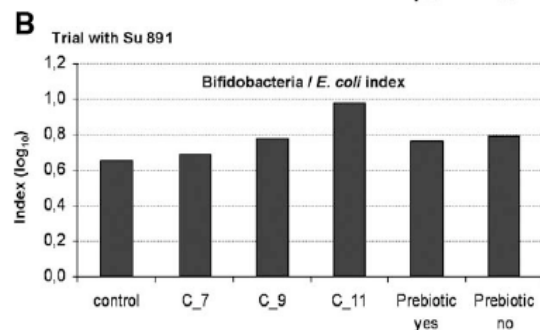
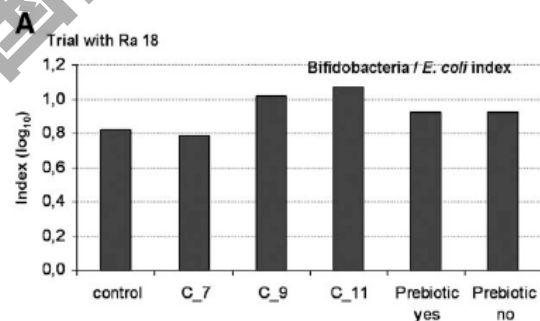
Effect of the different *Bifidobacterium* strains on bifidobacteria counts in caecum contents by plate counts and by direct semi-quantitative genus PCR

(Modesto *et al.*, 2009; *Livestock Science* 122:248-258)



饲喂不同益生素的断奶仔猪盲肠内容物中双歧杆菌和大肠杆菌的比例 (结果是双歧杆菌和大肠杆菌浓度的比值;虚线表示阈值限制)

Ratio of bifidobacteria to *E. coli* in caecum contents in weaning pigs fed different prebiotics (Results are ratio of the CFU of bifidobacteria to CFU of *E. coli*; dotted line indicates the control level arbitrarily chosen as threshold limit)



益生菌和益生素的剂量相关影响 (饲喂不同益生素的仔猪盲肠内容物中双歧杆菌和大肠杆菌的比例)

Dosage-related effects of probiotics or synbiotics (ratio of bifidobacteria to *E. coli* in caecum contents for pigs fed different probiotics)

Response of Nursery Pigs to a Synbiotic Preparation of Starch and an Anti-*Escherichia coli* K88 Probiotic[∇]

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保育猪对淀粉和抗大肠杆菌K88益生菌的合生素制备物的反应



试验设计

Experimental design

- 40头17日龄断奶仔猪随机分为四个处理 Forty 17-day-old weaned piglets were randomly assigned to four treatments:
 - 处理 1, 正对照日粮(**C**), 不含益生菌(**PRO**)或生土豆淀粉(**RPS**); 但含有饲用抗生素。 Treatment 1, positive-control diet (**C**), no probiotics (**PRO**) or raw potato starch (**RPS**) but containing in-feed antibiotics;
 - 处理 2, 益生菌组, 无抗生素, 50:50 比例的*E. coli* 菌株(**PRO**)(UM-2 和 UM-7)的益生菌混合物。 Treatment 2, probiotic, no feed antibiotics plus a 50:50 mixture of probiotic *E. coli* strains (UM-2 and UM-7) (**PRO**);
 - 处理 3, 14% RPS, 无抗生素(**RPS**); Treatment 3, 14% RPS, no antibiotics (**RPS**);
 - 处理4, 14% RPS 和 50:50 比例的*E. coli* 菌株 (UM-2 and UM-7)益生菌混合物; 无抗生素(**PRO-RPS**) Treatment 4, 14% RPS plus a 50:50 mixture of probiotic *E. coli* strains (UM-2 and UM-7), no antibiotics (**PRO-RPS**)
- 在试验的第7天, 用病原性大肠杆菌K88菌株进行攻毒(24日龄猪); 试验的第10天后施行安乐死(35日龄猪)
Pigs were challenged with pathogenic *E. coli* K88 strains on day 7 of the experiment (24-day-old pigs) and euthanized on day 10 of the experiment (35-day-old pigs)

感染后使用合益素改善了仔猪的生产性能和粪便评分

Growth performance and fecal score is improved with the synbiotic post-infection

	对照组 Control	益生菌 Probiotics	生土豆淀粉 (益生元) Raw potato starch (prebiotic)	益生菌 + 益生元 Probiotics + Prebiotic
初始体重 Start BW, kg	4.6	4.7	4.8	4.9
末重 Final BW, kg	5.8	5.9	5.9	6.4
感染后日增重(g) Daily gain (g) after infection	109	129	94	153
感染后日采食量(g) Daily feed intake (g) after infection	225	231	185	265
感染后肉料比 Gain to feed, after infection	0.47	0.55	0.49	0.60
粪便评分, 感染后48-96 小时 Fecal score, 48-96 h after infection	0.99	1.23	1.39	0.99

粪便评分: 0, 正常粪便; 1, 轻度腹泻; 2, 腹泻; 3, 严重腹泻

Fecal score: 0, normal feces; 1, mild diarrhea; 2, diarrhea; 3, severe diarrhea

Krause et al. (2010)

T-RFLP法分析回肠食糜菌群组成的划分

T-RFLP analysis-based hierarchical microbial composition of ileum digesta

Taxon	Microbial level (%) ^b				SEM ^a
	C	PRO	RPS	PRO-RPS	
Phylum <i>Bacteroidetes</i> 拟杆菌门分类	30.4	30.2	30.9	29.0	0.40
Class unclassified <i>Bacteroidetes</i>	1.4	1.2	1.9	0.0	0.40
Phylum <i>Firmicutes</i> 硬壁菌门分类	63.1	62.3	62.1	64.6	0.57
Class <i>Bacilli</i>	9.7	13.6	9.7	12.1	0.96
Order <i>Lactobacillales</i>	9.7	13.6	9.7	12.1	0.96
Class <i>Clostridia</i>	80.3	75.7	80.6	80.5	1.19
Order <i>Clostridiales</i>	61.0 ^A	61.5 ^A	56.5 ^{AB}	47.7 ^B	3.20
Order unclassified <i>Clostridia</i>	19.3 ^{AB}	14.2 ^A	24.1 ^{BC}	32.9 ^C	3.98
Class unclassified <i>Firmicutes</i>	3.1	3.0	1.9	2.0	0.32
Phylum <i>Actinobacteria</i> 放线菌门分类	0.3	0.0	0.0	0.7	0.17
Class <i>Actinobacteria</i>	0.3	0.0	0.0	0.7	0.17
Subclass <i>Coriobacteridae</i>	0.3	0.0	0.0	0.7	0.17
Order <i>Coriobacteriales</i>	0.3	0.0	0.0	0.7	0.17
Phylum <i>Proteobacteria</i> 变形菌门分类	4.8	5.9	5.6	4.0	0.43
Class <i>Epsilonproteobacteria</i>	0.7	1.2	0.9	0.0	0.25
Order <i>Campylobacteriales</i>	0.7	1.2	0.9	0.0	0.25
Class <i>Delta</i> proteobacteria	0.7	0.0	0.9	0.0	0.23
Order <i>Desulfovibrionales</i>	0.7	0.0	0.9	0.0	0.23
Class <i>Gamma</i> proteobacteria	1.7	2.4	1.4	1.3	0.25
Order <i>Pasteurellales</i>	0.3	0.0	0.5	0.0	0.12
Order <i>Enterobacteriales</i>	1.4	2.4	0.9	1.3	0.32
Class <i>Beta</i> proteobacteria	1.4	1.8	1.9	2.0	0.13
Order <i>Burkholderiales</i>	1.0	1.2	1.4	1.3	0.09
Order unclassified <i>Beta</i> proteobacteria	0.3	0.6	0.5	0.7	0.09
Class <i>Alphaproteobacteria</i>	0.0	0.0	0.0	0.0	0.00
Order unclassified <i>Alphaproteobacteria</i>	0.0	0.0	0.0	0.0	0.00
Class unclassified <i>Proteobacteria</i>	0.3	0.6	0.5	0.7	0.09
Phylum <i>Lentisphaerae</i> 黏胶球形菌分类	0.3	0.6	0.5	0.7	0.09
Class <i>Lentisphaerae</i>	0.3	0.6	0.5	0.7	0.09
Order <i>Victivallales</i>	0.3	0.6	0.5	0.7	0.09
Phylum unclassified <i>Bacteria</i> 非典型菌群分类	0.3	0.0	0.0	0.0	0.08

^a Pooled standard error of the mean.

^b Means within rows without a common letters differ ($P < 0.05$).

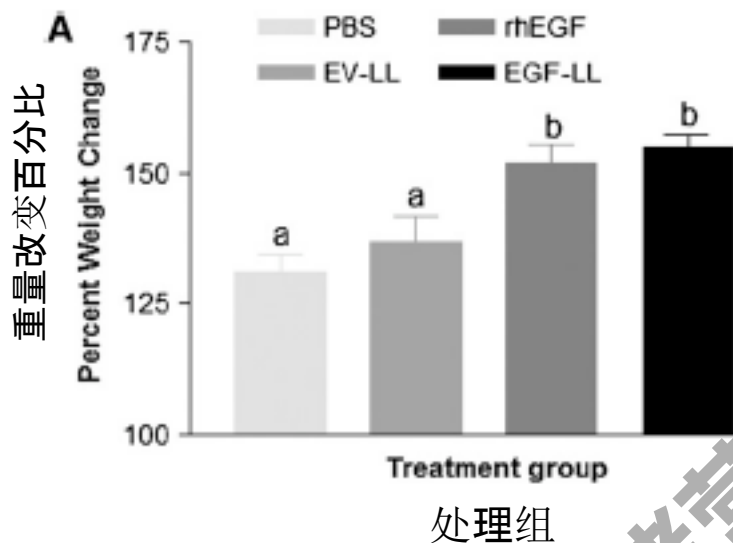
降低断奶后腹泻的一种合生素方案

A synbiotic approach to reducing post-weaning diarrhea

- 体内研究表明，在预防断奶后大肠杆菌病方面，选择大肠杆菌属益生菌，与生土豆淀粉结合能有效对抗大肠杆菌K88。 This study demonstrated *in vivo* that the selection of probiotic *E. coli* strains against *E. coli* K88 is effective in preventing post-weaning colibacillosis when fed in conjunction with raw potato starch
- 选择同一基因种属的益生菌菌株来排除病原菌的一个优势在于这种微生物通常在肠道中占据相同的位点。 An *advantage* of selecting probiotic strains of the same genus and species as the pathogen to exclude is that the organisms typically occupy the same niche in the gut
- 使用大肠杆菌作为益生菌的缺点：如果试图在饲料中获得批准添加大肠杆菌，通常被认为在安全和监管方面的障碍会比较大。 The *disadvantage* of using *E. coli* as a probiotic is that it is not generally considered safe and regulatory hurdles may be higher if attempting to gain approval for inclusion in feeds

设计细菌来表达表皮生长因子(EGF): 益生菌的附加值

Bacteria engineered to express epidermal growth factor: a 'probiotic' with added value

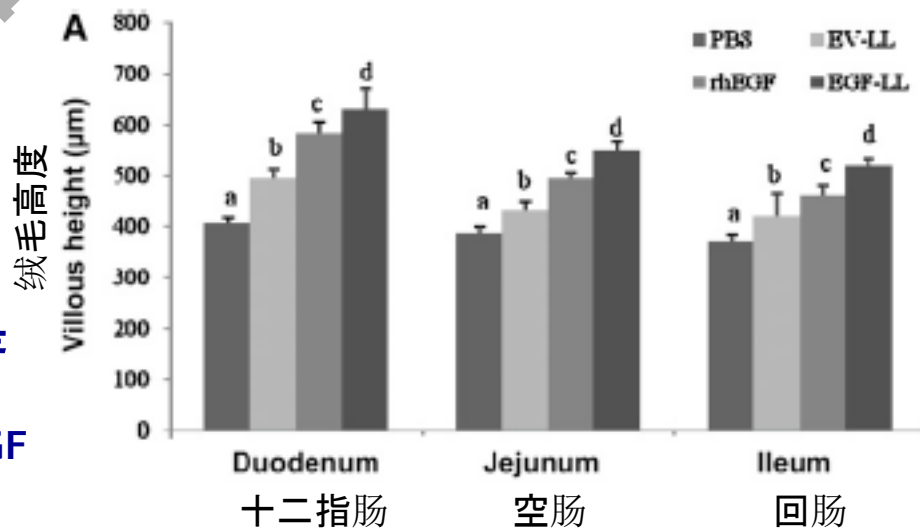


Generation of epidermal growth factor-expressing *Lactococcus lactis* and its enhancement on intestinal development and growth of early-weaned mice¹⁻³

Queenie CK Chung, Zongfei Yuan, Paul W Dyce, De Wu, Kees DeLange, and Julang Li

Am J Clin Nutr 2000;59:871-9.

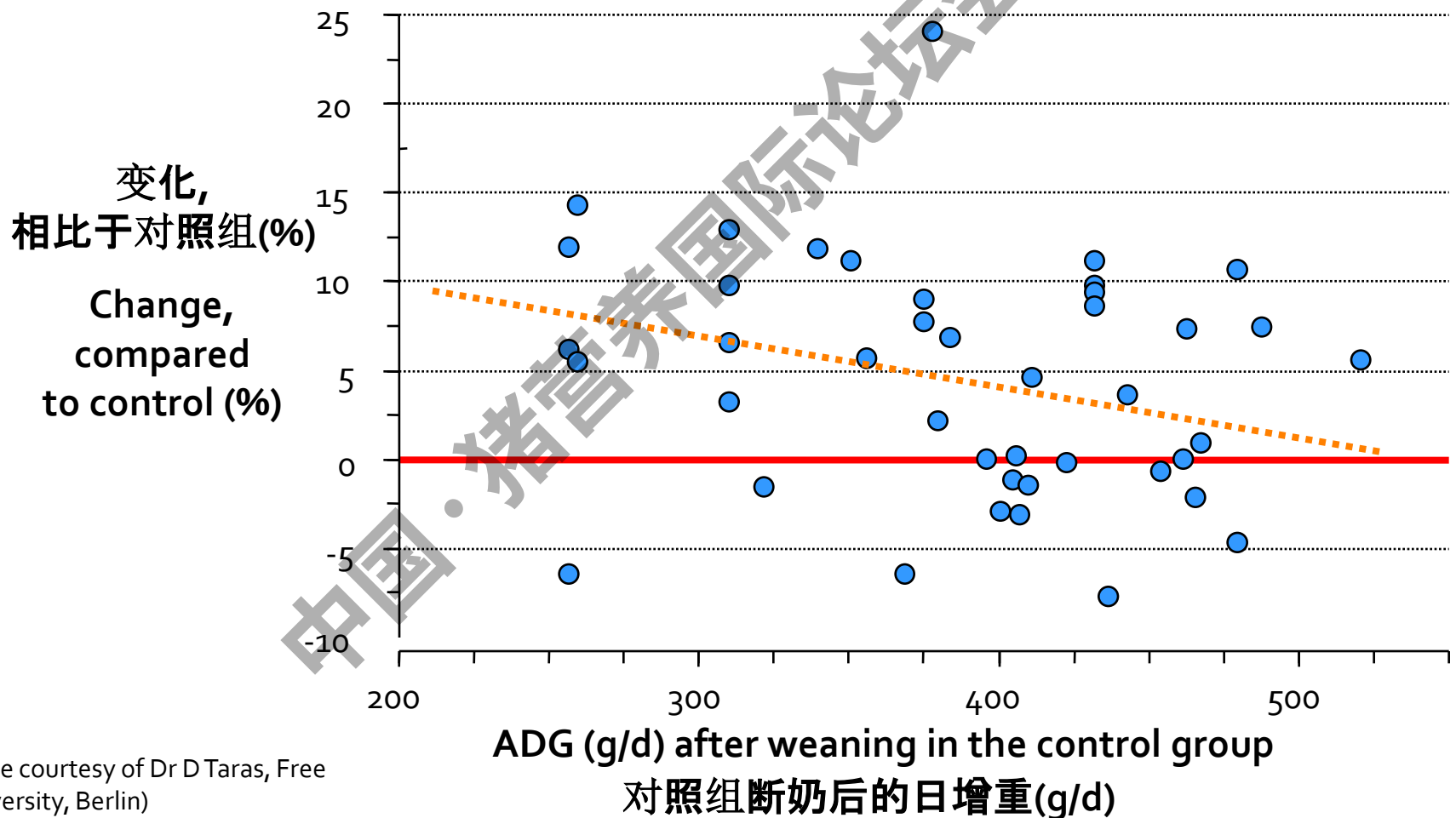
由乳酸乳球菌表达的表皮生长因子及其提高早期断奶小鼠肠道发育和生长



在有无EGF情况下, 老鼠口服生理盐水或是乳酸乳球菌 Mice orally gavaged with saline (PBS) or *Lactococcus lactis* (LL) with/without EGF

同行评估的试验: 断奶后益生菌的添加

Peer reviewed trials: probiotics after weaning (1993 - 2006)



结论和可用的信息

Conclusions and take-home messages

- 胃肠道——复杂的，生态环境，在那里共生体和致病菌与宿主共存，从而影响宿主的免疫功能； Gastrointestinal tract - complex, ecological environment where commensals and pathogens co-exist (most of the time) with the host to influence host immune function
- 抗生素耐药性，禁用抗菌药物，公司/消费者担忧，再一次将注意力聚焦在饲料策略的选择上（饲料成分，添加剂和管理），以利于最佳的胃肠道健康和肠道疾病的控制。 Antibiotic resistance, bans on antimicrobials, company/consumer concerns, have refocused attention on alternative feed strategies (ingredients, additives, management) for optimum gastrointestinal tract health and (or) control of enteric disease
- 需要对日益增长的消费者呼声及具福利意识的工业进行回应。 Need to respond to an increasingly consumer-responsive, welfare-conscious industry
- 必须继续研究新的产品和新的原料 (或者对于相同的产品或原料的不同的、新的使用方法) 。 Search for new products, new ingredients (or different/novel ways of using the same products or ingredients) must continue
- 带有商业性质的基础的和应用性的混合研究。 Mix of basic/applied research with commercial relevance