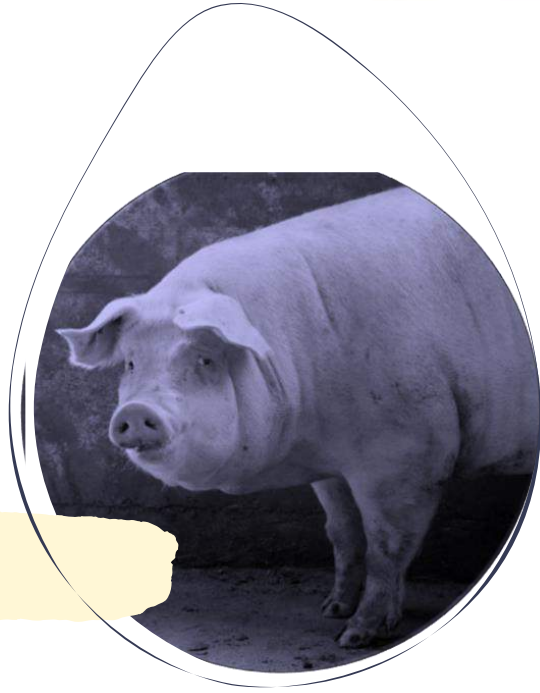
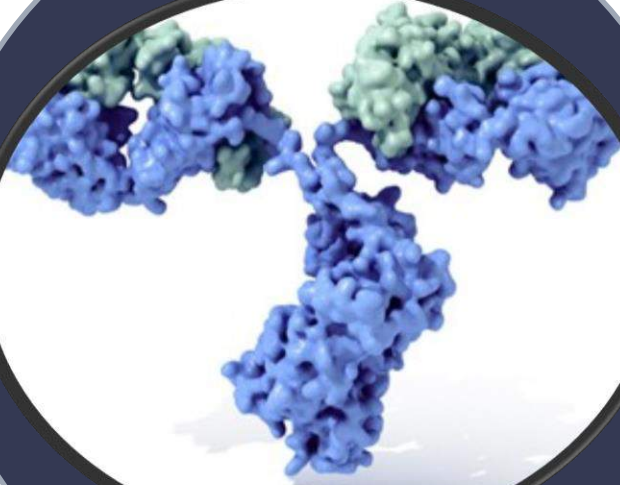


¿Cómo vamos?

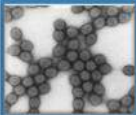
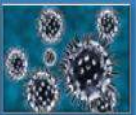



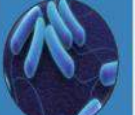



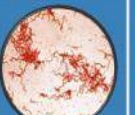

Depende.....

Tengo diarreas de todos los colores hasta No me va mal poniendo aditivos....muchos aditivos





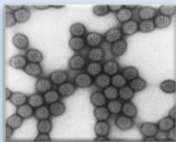

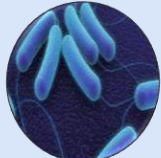
Estrategias inmunológicas

										
NO	NO	NO	SI	SI	SI	SI	SI	SI	NO	NO
Rota A. Importación de USA. Parenteral			Parenteral 8 registradas	Parenteral 2 registradas	Parenteral (Toxoide) 4 registradas	Parenteral (Toxoide) 2 registradas	Parenteral	VO 1 registrada		

								
Mycoplasma hyopneumoniae	A. pleuropneumoniae	B. bronchiseptica	P. multocida	H. parasuis	E. rhusiopathiae	Aujeszky	PCV2	SIV
Lechón	SI	SI	SI	SI	SI	SI	SI	SI
13 registradas VP	3 registradas VP	12 registradas VP	4 registradas VP	4 registradas VP	3 registradas VP	15 registradas VP/VIN	4 registradas VP	3 registradas VP

¿QUE VACUNAS TENEMOS?

¿A QUIÉN VACUNAMOS?

	 Rotavirus	 TGE	 PDVE	 <i>E. coli</i>	 <i>E. Coli (VT)</i>	 <i>C. Perfrin. C</i>	 <i>C. Perfrin. A</i>	 <i>C. difficile</i>
Cerda	NO Rota A. Importación de USA. Parenteral	NO	NO	SI. Parenteral	No	SI. Parenteral (Toxoide)	SI. Parenteral (Toxoide)	SI. Parenteral (Toxoide)
Lechón	NO Rota A. Importación de USA. Oral o Parenteral	NO	NO	SI. Oral y Parenteral	Si Parenteral	SI. Parenteral (Toxoide)	SI. Parenteral (Toxoide)	NO

ENCALOSTRADO

PERO PARA VACUNAR A LAS CERDAS.....



- Manejo de camadas al nacimiento
- Adopciones coherentes
- N° de tetas
 - ✓ Tetas funcionales
 - ✓ Pezones íntegros
- ¿Cantidad de calostro?



Decide bien que vacunas usar

Diagnostico

Diagnostico,
diagnostico y
diagnostico.

Prestale atencion a
aquellos patogenos
mas importantes.

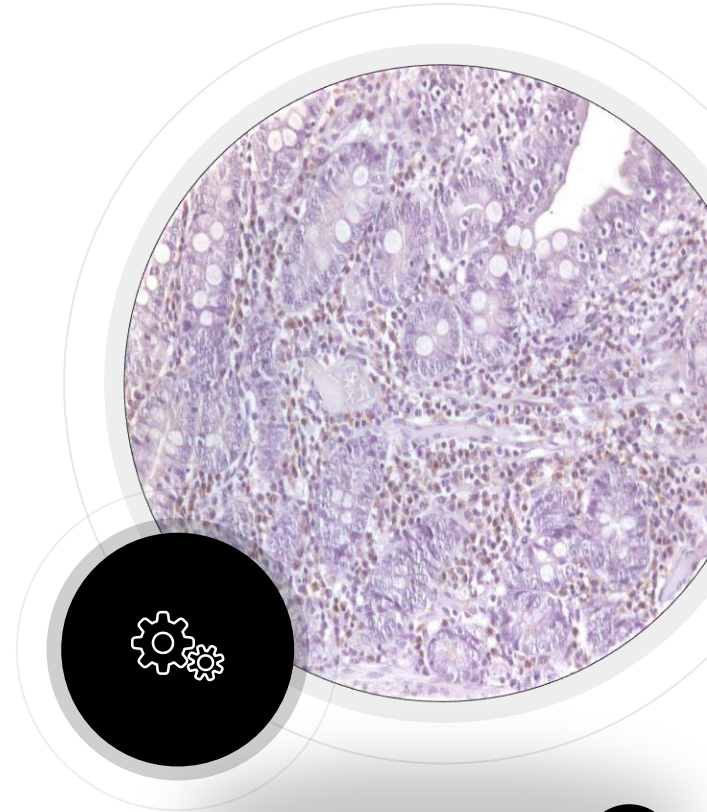
Cojugacion
respiratorio-
sistemico-digestivo

Importancia economica

Obvio.
Prestale mas
atencion a
aquellos que
mas dano
economico te
hacen

Estrategia

Combina
inmunidad
maternal con
inmunidad
adaptativa
siempre que
tengas un
buen
anclastroado.





¿Algún día tendremos
vacunas smart?

Optimicemos el sistema inmune

Ligado a un **DIAGNOSTICO CERTERO**

Escherichia coli inactivada con adhesina F4
Escherichia coli, inactivada con adhesina F5
Escherichia coli inactivada con adhesina F6
Escherichia coli inactivada con adhesina F41
Escherichia coli inactivada con adhesina F18ab
Escherichia coli inactivada con adhesina F18ac
Toxoide α de Clostridium perfringens tipo C
Toxoide β de Clostridium perfringens tipo C
Toxoide α de Clostridium perfringens tipo A
Toxoide β de Clostridium perfringens tipo A
Toxoide ϵ de C. perfringens tipo D
Rotavirus A
Rotavirus C
PEDV
TGEV

Escherichia coli inactivada con adhesina F4
Toxoide α de Clostridium perfringens tipo C
Rotavirus A

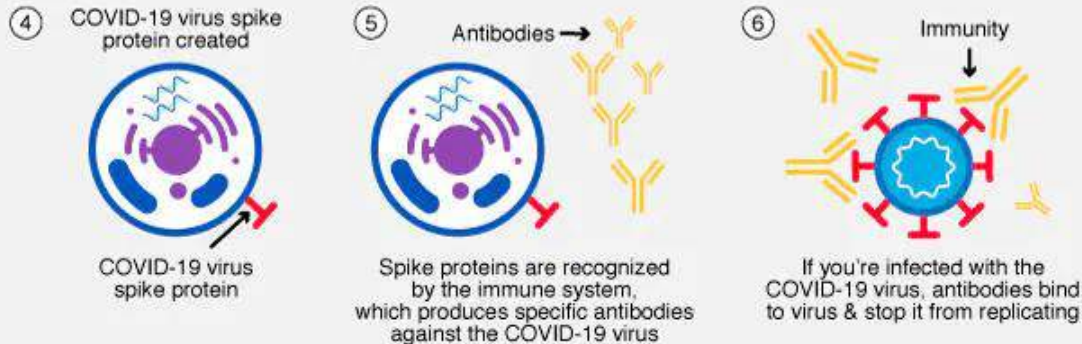
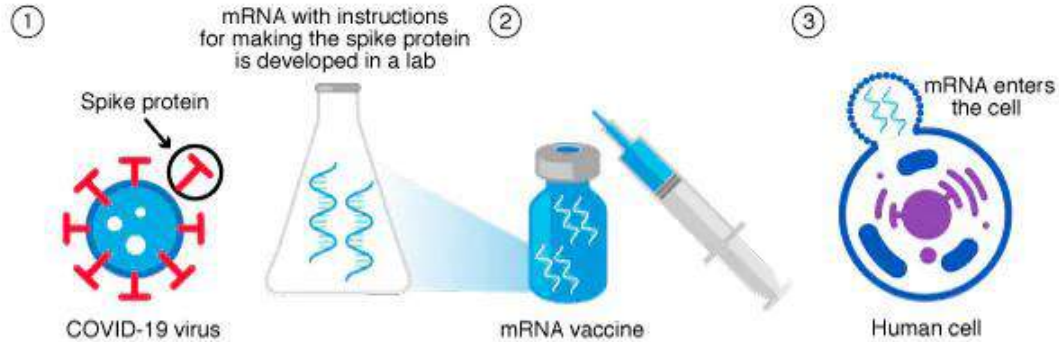
Escherichia coli inactivada con adhesina F4
Escherichia coli inactivada con adhesina F18ab

Rotavirus A
PEDV

Escherichia coli inactivada con adhesina F4
Toxoide α de Clostridium perfringens tipo C
Toxoide α de Clostridium perfringens tipo A
Toxoide β de Clostridium perfringens tipo A
Rotavirus C



VACUNAS ARNm





Y de feedback no vamos a hablar?



Estrategia valida si no hay vacuna

Bien hecha, usando antibiotico, sin cultivo.

Desventaja: sabemos porque lo hacemos, sabemos frente a que queremos inmunizar el colectivo.....pero no sabemos en realidad que metemos ni que dosis.





// Y de AUTOVACUNAS?

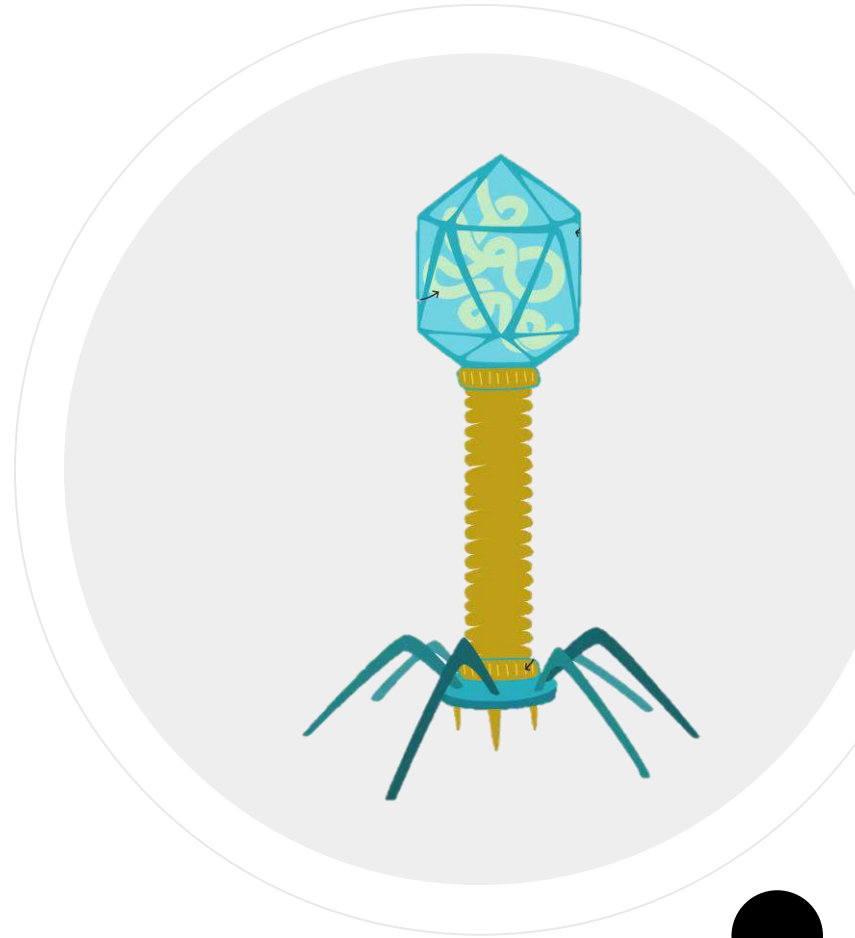
De nuevo estrategia valida si no hay vacuna

Pero desafortunadamente en algunos patogenos se ha convertido en la norma por la ausencia de vacunas comerciales





Fagos?



Review

Bacteriophage-Based Vaccines: A Potent Approach for Antigen Delivery

Alejandro González-Mora ¹, Jesús Hernández-Pérez ¹, Hafiz M. N. Iqbal ¹, Marco Rito-Palomares ¹ and Jorge Benavides ^{1,*}

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² Tecnológico de Monterrey, School of Medicine and Health Sciences, Ave. Miramón Prieto 3000 Pte, Monterrey, N.L. 64710, Mexico; mrio@tec.mx

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Received: 31 July 2020; Accepted: 1 September 2020; Published: 4 September 2020



Abstract: Vaccines are considered one of the most important bioproducts in medicine. Since the development of the smallpox vaccine in 1796, several types of vaccines for many diseases have been created. However, some vaccines have shown limitations as high cost and low immune responses. In that regard, bacteriophages have been proposed as an attractive alternative for the development of more cost-effective vaccines. Phage-displayed vaccines consists in the expression of antigens on the phage surface. This approach takes advantage of inherent properties of these particles such as their adjuvant capacity, economic production and high stability, among others. To date, three types of phage-based vaccines have been developed: phage-displayed, phage DNA and hybrid phage-DNA vaccines. Typically, phage display technology has been used for the identification of new and protective epitopes, mimotopes and antigens. In this context, phage particles represent a versatile, effective and promising alternative for the development of more effective vaccine delivery systems which should be highly exploited in the future. This review describes current advances in the development of bacteriophage-based vaccines, with special attention to vaccine delivery strategies. Moreover, the immunological aspects of phage-based vaccines, as well as the applications of phage display for vaccine development, are explored. Finally, important challenges and the future of phage-based vaccines are discussed.

Keywords: bacteriophage; vaccines; phage display technology; immunological mechanism; antigen delivery

Article

Bacteriophages as Potential Tools for Use in Antimicrobial Therapy and Vaccine Development

Rosa Zafrańska-Pajek ^{1,2} and Rafal Pajek ^{2,3}

¹ Department of Microbial Biotechnology and Biochemistry, Chemical Faculty, Łódź University of Technology, Naumborska 11, 52-070 Łódź, Poland; Rosa.zafranska@p.lodz.pl

² Bio-Inhaled Cores, Łódź University of Technology, Naumborska 11, 52-070 Łódź, Poland

³ Correspondence: rafal.pajek@p.lodz.pl; Tel.: +48-42-635-1000

Abstract: The constantly growing number of people suffering from bacterial, viral or fungal infections, genetic diseases, and cancers pushes the search for innovative methods of disease prevention and treatment, especially based on vaccines and targeted therapy. An additional problem is the lack of those to be used resulting from the increasing resistance of bacteria to conventionally used antibiotics. Conventional vaccines based on bacteria or viruses are common and are generally effective in preventing and controlling various infectious diseases in humans. However, there are problems with the stability of these vaccines, their transport, targeted delivery, side effects, and side effects. In this context, bacteriophage therapy based on in vivo application of bacteriophages currently offers a chance for a breakthrough in the treatment of bacterial infections. Phages are not infectious and pathogenic to humans, and do not cause diseases in human body. Furthermore, bacterial viruses are sufficient to cause infections with potential adverse effects, easy to transport, and store. They can also be produced on a large scale without inhibitors. In recent years, they have also provided an ideal platform for the design and production of phage-based vaccines to induce protective host immune responses. The most promising in this group are phage-displayed vaccines, allowing for the display of immunogenic peptides or proteins on the phage surface, or phage DNA vaccines, impossible for expression of target genes (protein, protective antigen) incorporated into the phage genome. Phage vaccines including the production of specific antibodies may in the future protect us against infectious diseases and constitute an effective treatment tool to fight cancer. Moreover, personalized phage therapy can represent the greatest medical achievement that has been. This review demonstrates the latest advances and developments in the use of phage vaccines to prevent human infections, disease, phage-based therapy, including clinical trials, and personalized treatment adapted to the patient's needs and the type of bacterial infection. It highlights the advantages and disadvantages of experimental phage therapy and, at the same time, reviews its great potential in the treatment of various diseases, especially those resistant to commonly used antibiotics. All the analyses performed look at the rich history and development of phage therapy over the past 200 years.



Citation: Zafrańska-Pajek, R.; Pajek, R. Bacteriophage as Potential Tools for Use in Antimicrobial Therapy and Vaccine Development. *Pharmaceutics* **2021**, *13*, 182. <https://doi.org/10.3390/ph1309182>

Academic Editor: Sergio Martínez

Received: 1 March 2021
Accepted: 2 April 2021
Published: 4 April 2021

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Keywords: phages; phage-based vaccines; phage display technology; phage DNA vaccines; bacterial infections; phage therapy

1. Introduction

The increasing number of antibiotic-resistant bacteria correlates with increased healthcare costs, morbidity, and mortality worldwide. The World Health Organization (WHO) Global Antibiotic Resistance Strategy 2019–2035 states that antibiotic resistance is one of the greatest threats to public health and global development. In 2014, WHO prepared the first revision of the International Statistical Classification of Diseases and Related Health Problems, designating 17 disease categories (Supplementary Material, Table S1) [1]. In addition, WHO compiled a global list of antibiotic-resistant bacteria to identify the research and development of new drugs against resistant bacteria. The analysis showed that 94% of pathogens



Probioticos

Probioticos

Cultivos vivos de bacterias y levaduras (algunos no contienen germenes vivos, solo paredes de levaduras)

Modo de accion: establecer competencia con bacterias patogenas o saprófitas con potencial patogeno.

Resultados: variables en ocasiones inconsistentes.

Fase de utilización: LACTACION Y TRANSICION

- Compiten con los microorganismos indeseables.
- Algunos producen ácidos grasos volátiles que ayudan a mantener un pH beneficioso para el desarrollo de bacterias ácido lácticas en detrimento de coliformes, *Salmonella* y *Clostridium*.
- Producen sus propias bacteriocinas, una familia de péptidos bioactivos con actividad bacteriostática sobre gérmenes Gram positivos (y probablemente sobre algunos Gram negativos).
- Pueden mejorar la inmunidad intestinal evitando la acción de ciertos vectores, tales como rotavirus, organismos inductores de numerosos procesos diarreicos.
 - Reduce la concentración en plasma de ciertos metabolitos perjudiciales tales como amoniaco
 - y endotoxinas.

Especies

- *Bacillus coagulans*
- *Bacillus cereus*
- *Bacillus licheniformis*
- *B. licheniformis* + *B. subtilis*
- *Bacillus toyoi*
- *Bifidobacterium lactis* (**mejora funciones inmunes como fagocitosis o inm. celular**)
- *Bifidobacterium animalis* (**protege ID de citocinas preproducidas por infec. E.coli**)
- *Brevibacterium lactofermentum*
- *Clostridium butyricum* (**produce grandes cantidades de butirato, altera pH**)
- *Enterococcus faecium* (**inhibe la adhesión de E. coli F4**)
- *Escherichia coli* productor de colicina (**reduce la adhesión de E. coli F4**)
- *Lactobacillus rhamnosus* (**protege ID de citocinas preproducidas por infec. E.coli**)
- *Lactobacillus casei*
- *Lactobacillus acidophilus*
- *Lactobacillus fermentum* (**inhibe la adhesión de E. coli F4**)
- *Lactobacillus* + *Streptococcus*
- *Sacharomyces cerevisiae* + *Lactobacillus acidophilus* + *Streptococcus faecium*
- *Saccharomyces boulardii* + *B. cereus*
- *Streptococcus faecium*





Prebioticos

Sustancias fermentables que promueven el crecimiento selectivo de bacterias beneficiosas

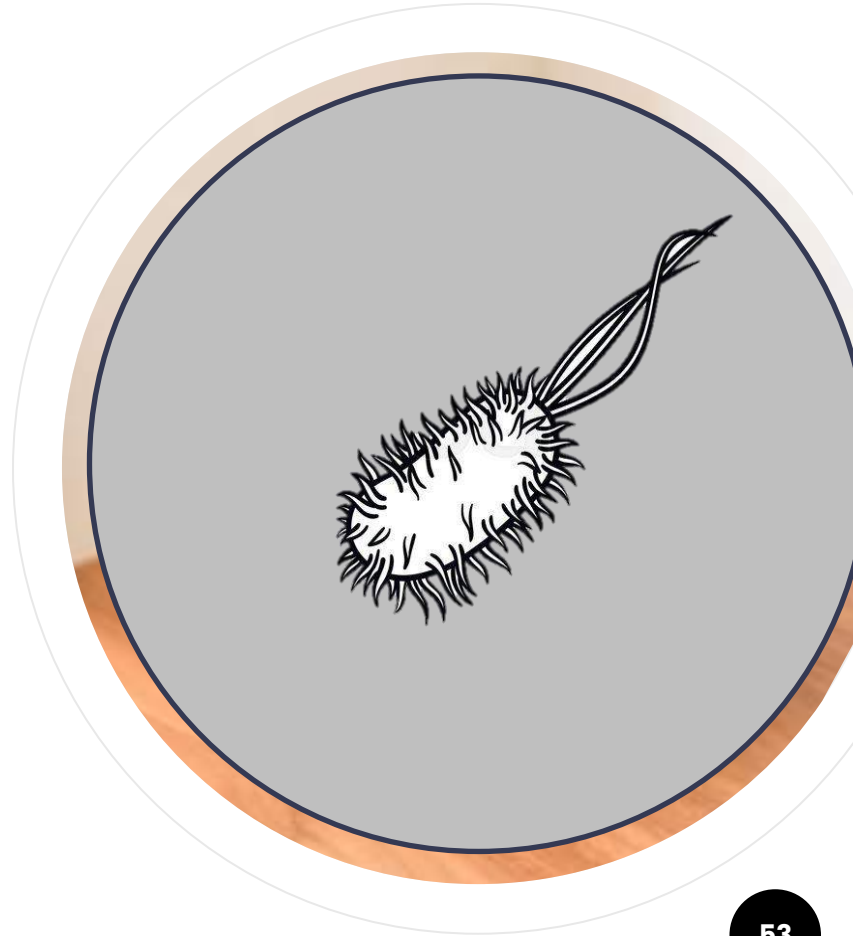
Lactosa: el ejemplo en la naturaleza

Hemicelulosa, oligosacaridos, inulina, glucanos de cadena corta, fructosanos y arabinanos.

Almidon retrogrado: calentado y enfriado rapidamente.

Fase de utilización: TRANSICIÓN

.



Especies

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Fructooligosacáridos

Transgalactooligosacáridos

Almidón de patata

Especies

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- *Lactobacillus acidophilus*
- *Lactobacillus fermentum*
- *Streptococcus faecium*
- *Lactobacillus + Streptococcus*
- *Escherichia coli* probiótica
- *Brevibacterium lactoferum*
- *Bacillus coagulans*
- *Bacillus cereus*
- *Bacillus licheniformis*
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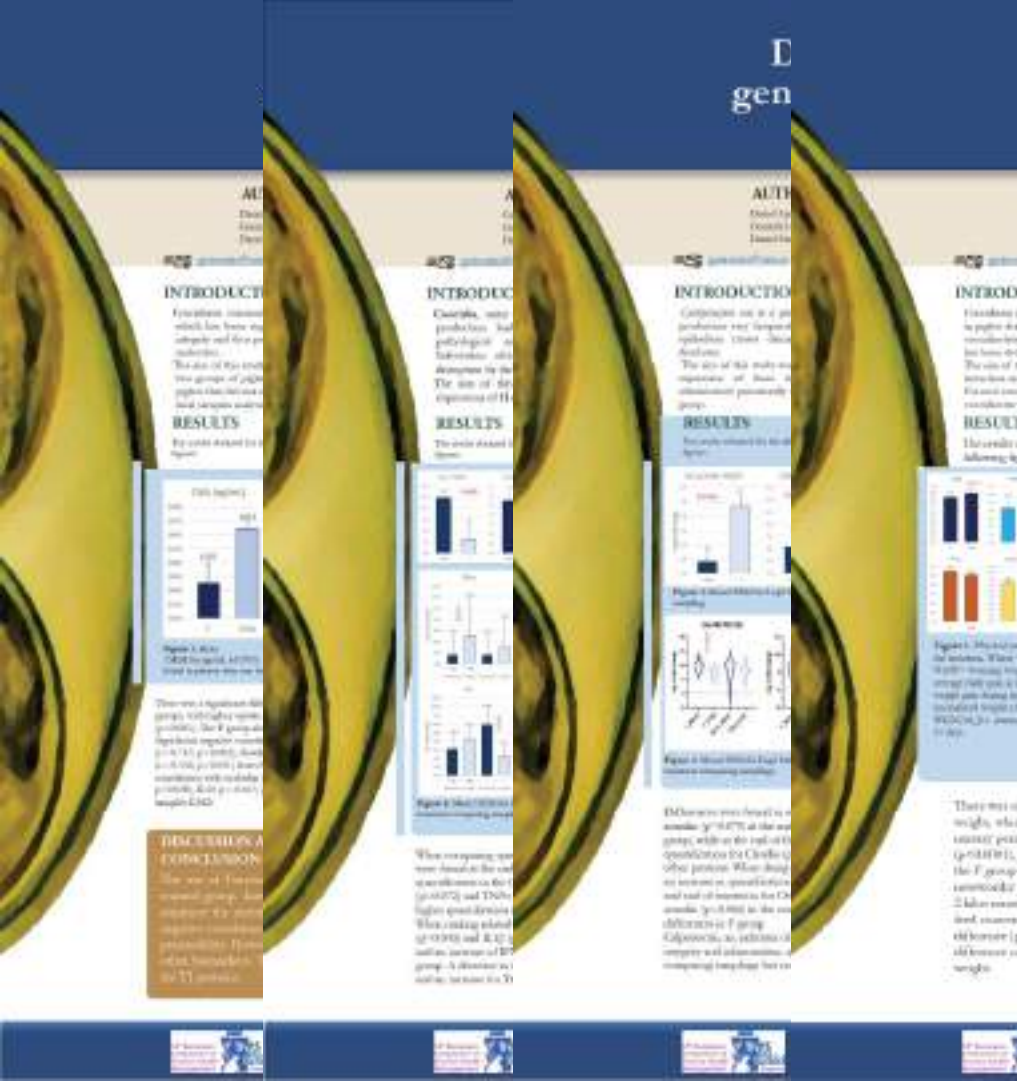
Simbiótico = Prebiótico
+ Probiótico





¿Parásitos?





D gen

ABSTRACT
 Objective
 Design
 Setting
 Duration
 Participants
 Measurements and
 Main Results

INTRODUCTION

Excessive iron intake, which has been reported in piglets, may lead to iron overload. The aim of this study was to evaluate the effect of iron overload on the growth and mortality of piglets.

RESULTS

By using a piglet model, we found that iron overload significantly increased mortality and reduced growth.

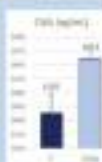


Figure 1. Mortality (%) in piglets with iron overload.

There was a significant difference in mortality between the iron overload group and the control group ($P < 0.05$). The mortality rate was significantly higher in the iron overload group ($P < 0.05$).

DISCUSSION AND CONCLUSIONS

The results of this study suggest that iron overload in piglets leads to increased mortality and reduced growth. This finding is important for the management of iron overload in piglets.

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Growth and mortality in piglets treated with parenteral tofrazuril and iron



Guillermo Ramos¹, Ana B. Gonzalez-Guijarro, Elisa Y¹, Hernández-Rodríguez¹, David Espigares¹

¹University of Murcia, Espigares, Murcia, Spain (e-mail: david.espigares@um.es)

Background and objectives

Previous studies have demonstrated that iron overload in piglets can lead to mortality. The aim of this study was to evaluate the effect of iron overload on the growth and mortality of piglets treated with parenteral tofrazuril and iron.

Material and methods

A total of 100 piglets were randomly divided into two groups: a control group (n = 50) and a treatment group (n = 50). The treatment group received parenteral tofrazuril and iron. The control group received only parenteral iron. The results of the following study are presented.

There was no difference in mortality between the iron overload group and the control group ($P > 0.05$). The mortality rate was significantly higher in the iron overload group ($P < 0.05$).

Results

There was no difference in mortality between the iron overload group and the control group ($P > 0.05$). The mortality rate was significantly higher in the iron overload group ($P < 0.05$).



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Table 1. Mortality (%) in piglets with iron overload.

Group	Mortality (%)	
	Iron overload	Control
n	50	50
Mortality (%)	10	5
P-value	0.05	0.05

Discussion and conclusion

The results of this study suggest that iron overload in piglets leads to increased mortality and reduced growth. This finding is important for the management of iron overload in piglets.

References

1. Ramos G, Gonzalez-Guijarro AB, Y E, Hernández-Rodríguez E, Espigares D. Growth and mortality in piglets treated with parenteral tofrazuril and iron. *Proceedings of the 12th International Conference on Pig Production and Health*, 2014; 12: 1-4.

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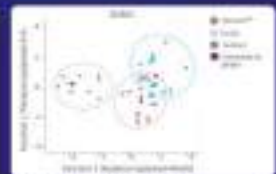


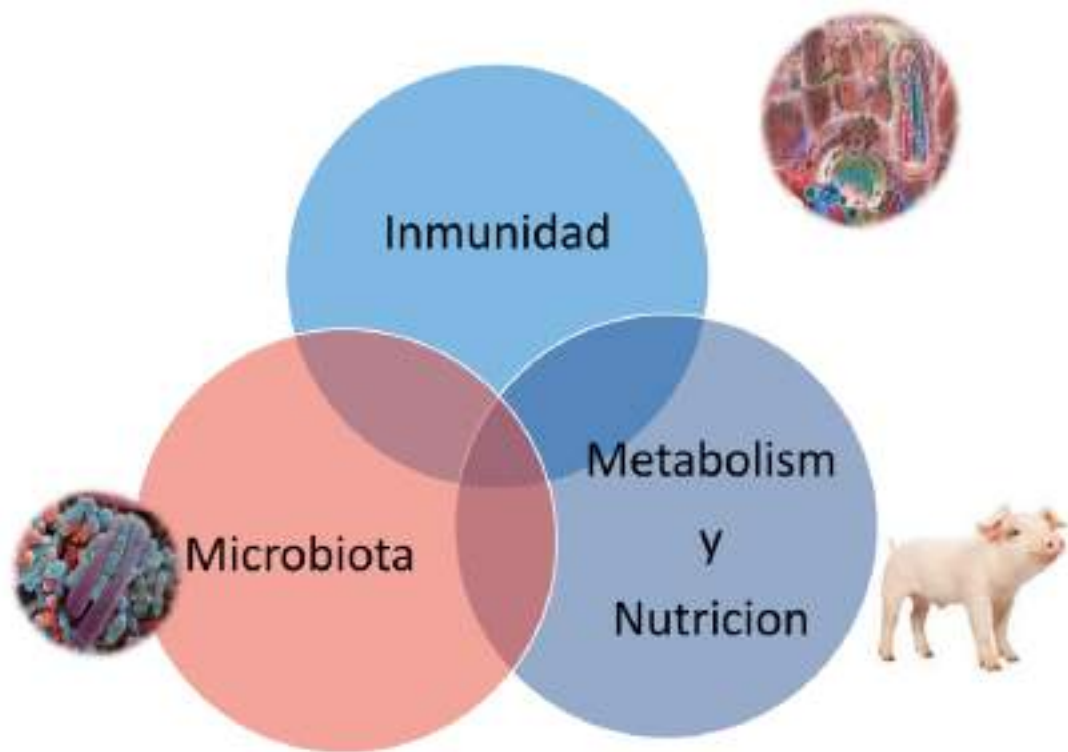
Figure 1. Mortality (%) in piglets with iron overload.



Nuevas perspectivas

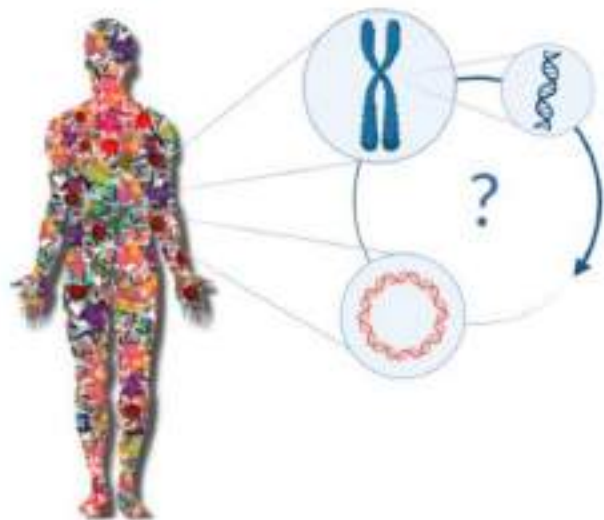
Nuevos conceptos. Microbiota

La Salud es un equilibrio en el Holobiont

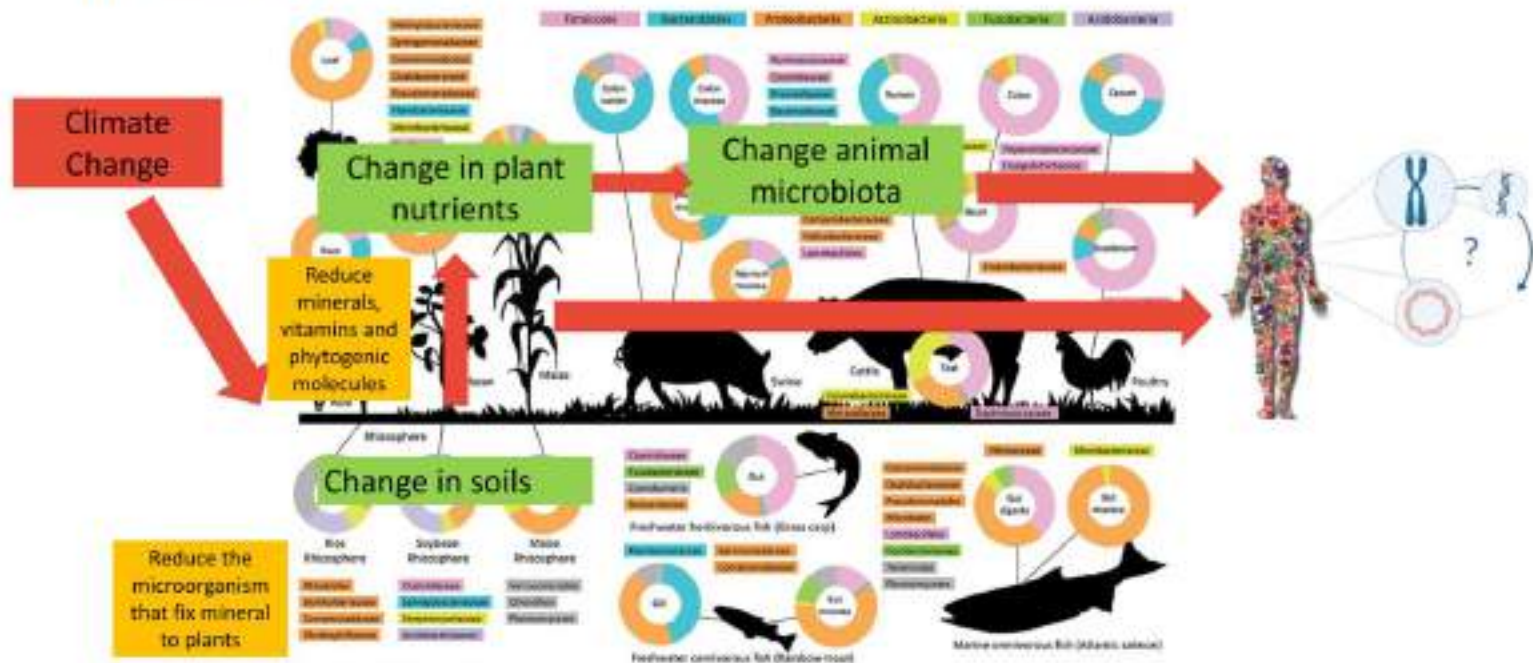


The Holobiont concept for sustainability

The holobiont theory consider the host and microbiota as a unique entity where one can interact with each other in cooperation or mutualism to stablish a balance in order to have the better fitness of both systems (Simon et al., 2019).



THE HOLOBIONT CONCEPT FOR SUSTAINABILITY





Nutraceuticos y +

Nutraceuticos

Suplementos alimentarios

Sustancias vegetales

Aceites esenciales de romero, menta, anís, canela, tomillo, ajo, ginseng, orégano

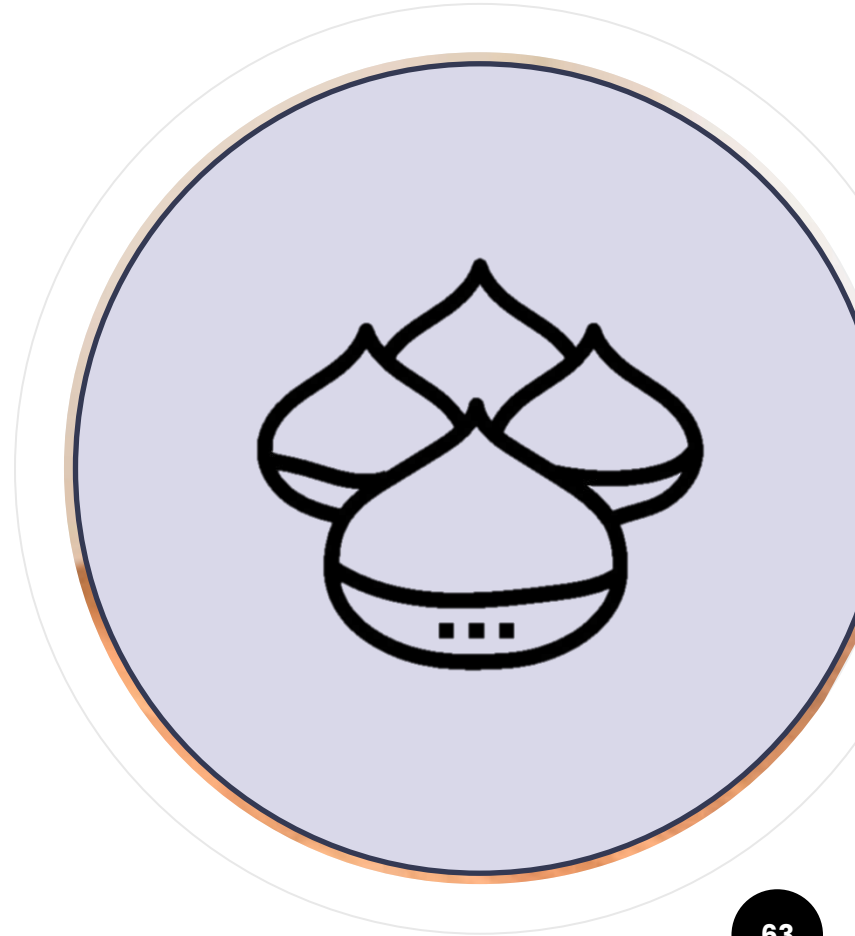
β -caroteno, luteína y xantenos, vitamina E: antioxidantes

Aceites de pescado ricos en ácidos grasos ω -3

Taninos

FASE DE UTILIZACION: TODAS

.



Inmunomoduladores

Anticuerpos

Huevo liofilizado conteniendo anticuerpos frente a rotavirus y *E. coli*

Yema de huevo desecada con Ac frente a *E. coli* enterotoxico

Citoquinas (experiencias en pollos)

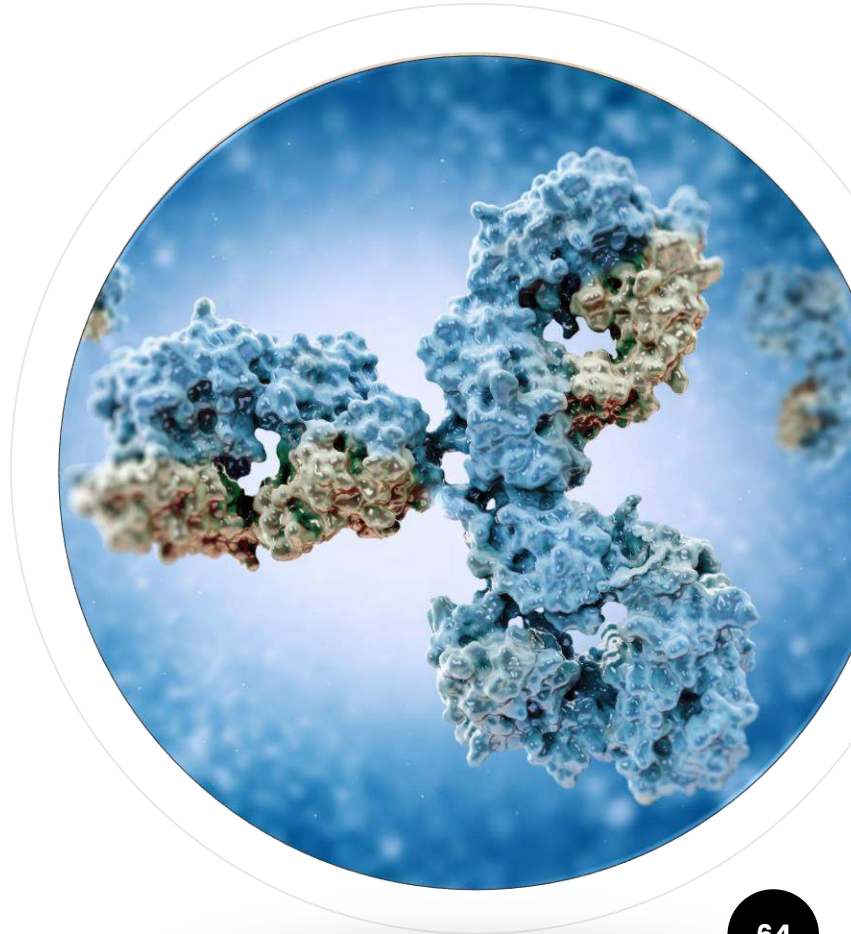
Proteínas plasmáticas liofilizadas

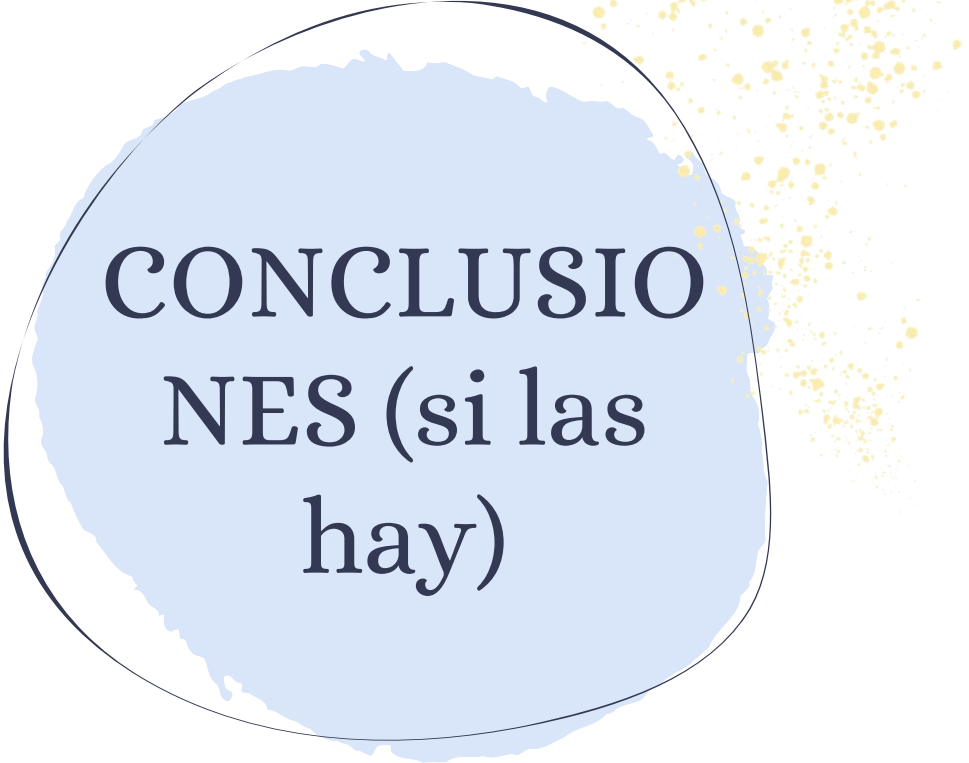
Contiene ciertas proteínas inmunoactivas

Péptidos antimicrobianos (más de 12 identificados en cerdos)

Acido linoleico conjugado: aumenta la producción de linfocitos T e IL-2.

FASES DE UTILIZACION: LACTACION Y TRANSICION.





CONCLUSIONES
(si las
hay)

8,850,000,000 €

AUTOABASTECIMIENTO: 212% (2021)

NO...NOS LO EXIGEN EL MERCADO Y EL
EQUIVALENTE A $\frac{3}{4}$ DE NUESTRO CONSUMO LO
VENDEMOS FUERA.....QUE SON MAS REACTIVOS A
ESTOS TEMAS QUE EL MERCADO INTERIOR



Esto no existe. Tenemos que componer el conjunto de medidas que mejor nos ayude en nuestra realidad...vacunas, probioticos....
hacen falta varias cosas



Nuestras herramientas

Diagnóstico
certero

Manejo
optimizado

Luego todo
lo demás

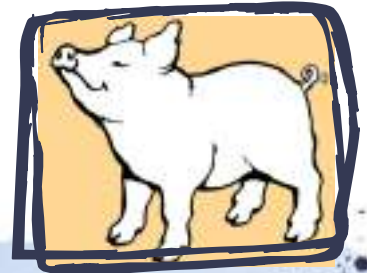
UNO DE LOS
COMPONENTES
CLAVE DE
CUALQUIER VACUNA

¿Qué es todo lo demás?

Vacunas, probióticos y prebióticos

Son las soluciones con mayor desarrollo tecnológico, científico y exigencias de la administración

Lo que no significa que nutraceuticos,
inmunomoduladores y otras estrategias
no vayan a ayudarnos





¿CUAL DE ESTAS SOLUCIONES
FUNCIONARA IGUAL QUE LOS
ANTIBIÓTICOS Y EL ZnO?

NINGUNA



MUCHAS
GRACIAS
POR LA
ATENCIÓN