GENETICALLY ENGINEERED LIVESTOCK: APPLICATIONS IN FOOD PRODUCTION AND MEDICINE

Anna Rey Garcia
June 2017

INTRODUCTION AND OBJECTIVES

The initial application of the genetically modified animals was to contribute in the basic research with the aim to study the function mechanisms of the organism and to achieve a better understanding of genes function.
A transgenic animal is one that has been genetically modified either through the insertion of exogenous genes, or from the elimination or modification of their own genes. The goal is to modify existing features or to add new ones.

The target of this review is to show the main applications of genetically modified animals. On the other hand, a second aim is to show the controversy generated by the use of these animals as well as the legislation that is responsible for its regulation.

METHODS OF MAKING TRANSGENIC ANIMALS

Originally, transgenic mammals were created through a technique called pronuclear microinjection.
The lack of efficiency of this technique has given place to research of new methods to obtain transgenic animals such as retroviral vectors or somatic cell nuclear transfer (SCNT).
Recent advances in genome editing have allowed the creation of designer engineered nucleases like ZFN, TALEN and CRISPR/Cas9. These nucleases allow a precise genome editing in livestock. Its mechanism of action is based on the creation of a double-stranded break in the DNA with the aim to stimulate the DNA repair pathway.

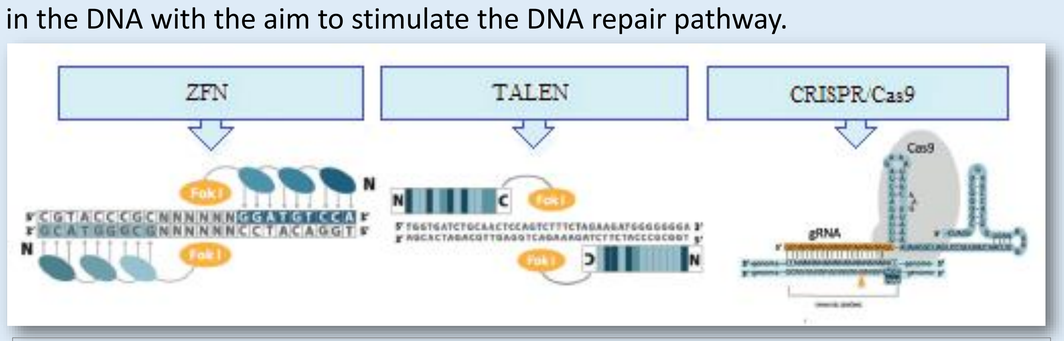


Figure 1. Structure of ZFN, TALEN and CRISPR/Cas9. From: Garcia i Pujol (2015)

APPLICATIONS OF GENETICALLY ENGINEERED LIVESTOCK

Models of disease

Livestock have been proposed to overcome the limitations of mice as models of disease because they share anatomical and physiological characteristics with humans. However, they have some limitations, such as production cost or time to be invested to develop similar diseases to those of humans.

- Pigs as models of cardiovascular diseases (ex. Atherosclerosis)
  Pigs as models of neurodegenerative diseases (ex. Alzheimer)

- Sheep as models of diseases of the respiratory system (ex: asthma, cystic fibrosis)

- Goats have been used in research on cystic fibrosis

Environment

Global animal phosphorus pollution is a serious and growing problem.
Monogastric animals can not digest phytate plant, so they required dietary supplementation with mineral phosphate.

Study

Golovan et al. (2001) have developed the phytase transgenic pig. The saliva of these pigs contains phytase, which allows a complete digestion of dietary phytate.

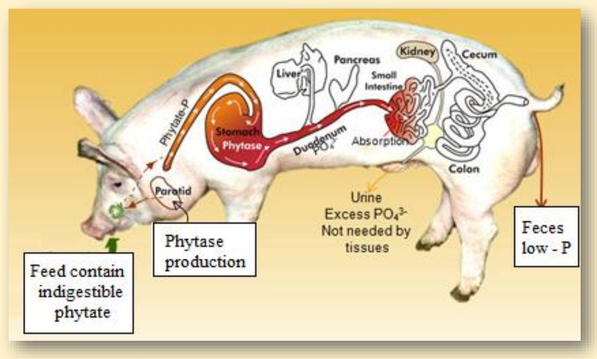
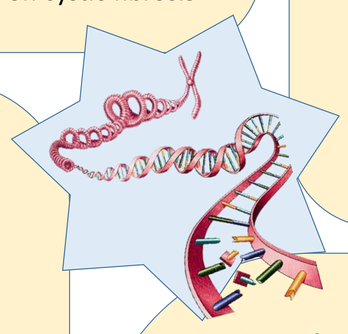


Figure 2. Phytase transgenic pig.
From: http://www.uoguelph.ca/enviropig/

Disease resistance



Why?

- **To solve a problem of animal welfare**
- **To prevent the spread of zoonotic diseases**
- **To reduce the use of antibiotics**

Studies: Calves more resistant to mastitis

Liu et al. (2013)	Liu et al. (2014)
Worked with lisostafina (enzyme with antibacterial activity)	Worked with human lysozyme (antimicrobial protein)
Integration through ZFNickases	Integration through ZFN
Target gene: β-casein locus	Target gene: β-casein locus

Growth and yield

In order to increase production many studies have been conducted to achieve an increase in muscle mass. Some studies have been working with the gene MSTN, which encodes for the miostatina, a protein that plays an important inhibitory role during muscle development.

Figure 3. Calves with MSTN biallelic mutations displayed the doubled-muscled phenotype. From: Luo et al. (2014)

Figure 4. Transgenic lamb with muscular hypertrophy.
From: Proudfoot et al. (2015)

Figure 5. Note that *MSTN*−/− pigs show wider back, fuller rump and thicker limbs.
From: Qian et al. (2015)

Moreover, AquaBounty Technologies created a transgenic salmon that grows twice as big and at a greater speed than conventional ones.

Figure 6. Differences in growth between AquAdvantage Salmon and conventional during the first three years of life.
From: AquaBounty Technologies

Studies	Species	Technique
Luo et al (2014)	Cattle	ZFN
Zhao et al. (2016)	Sheep	TALEN
Proudfoot et al. (2015)	Sheep and cattle	TALEN
Qian et al. (2015)	Pig	ZFN

CONTROVERSY AND LEGISLATION

Controversy

Pros	Cons
Improve animal health	Public resistance to GE technology
Reduce the use of antibiotics	Perceived lack of safety in food from GE animals
Decreased environmental impact of farming	Threat to the environment (introduction of modified genes into wild populations)

Legislation

The EU has established a legal framework to ensure the protection of human and animal health as well as the environment.

Regulation of evaluation and authorization of genetically modified food is determined by:
- Directive 2001/18 / EC
- Regulation (EC) Nº 1829/2003
- Regulation 503/2013

CONCLUSIONS

- The techniques to obtain genetically modified animals have advanced greatly in recent years.
- Thanks to the development of nucleases design, we can today mimic natural mutations by placing specific modifications in the genome.
- Many studies aim to produce transgenic animals for human consumption. However, most of these animals are only under investigation at present.
- Only AquAdvantage salmon has currently been approved for human consumption.
- Despite the advantages that genetically modified animals could pose, these studies can not come to everyday use until public opinion is not favourable.