



Genetically Modified (GM) Animals: Developments in Research and Policy Framework

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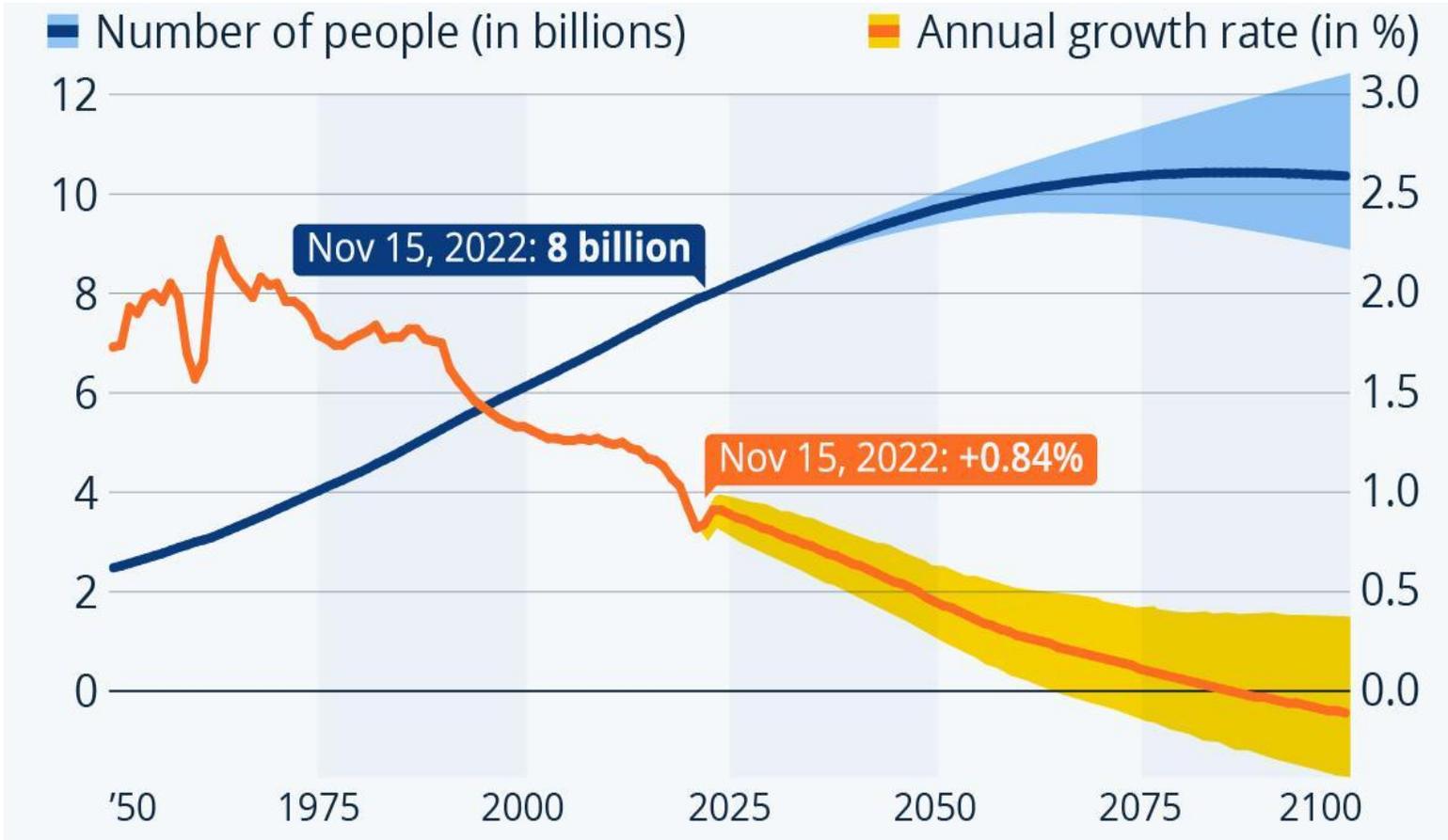
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Masaganang Agrikultura, Maunlad na Ekonomiya

The Global Challenge: Feeding the World Sustainably by 2050



Increase Food Production Without Expanding Agricultural Land

Reduce Growth In Demand for Food and Other Agricultural Products

Reduce Greenhouse Gas Emissions from Agricultural Production



Impact of Climate Change on Food Systems

Decreased arability



Fisheries



Hunger food security & nutrition



Reduced yields



Planting and harvesting changes



Emerging food risks

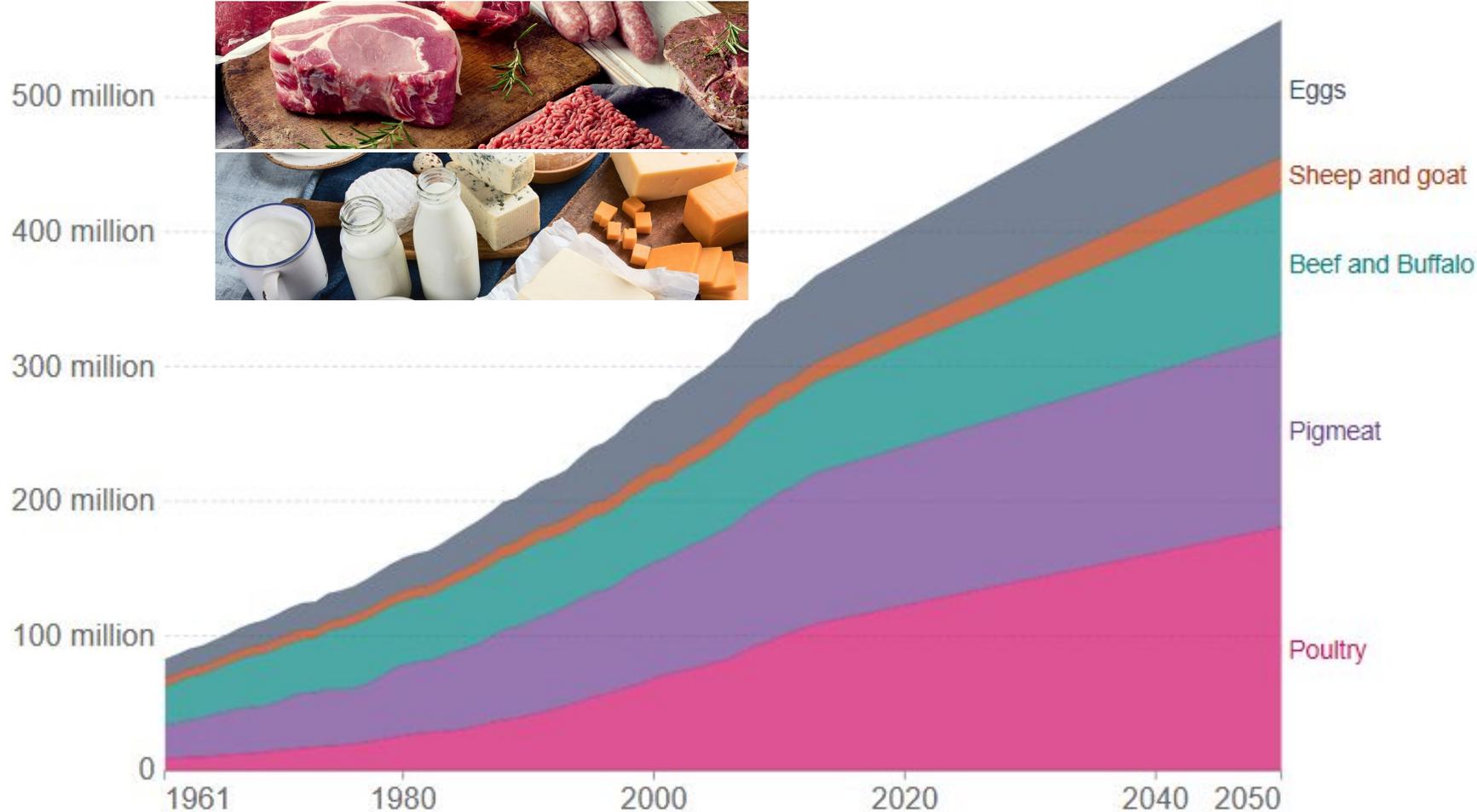


Increased irrigation



Global meat consumption, World, 1961 to 2050

Expressed in tonnes of meat. Data from 1961-2013 is based on published FAO estimates; from 2013-2050 based on FAO projections. Projections are based on future population projections and the expected impacts of regional and national economic growth trends on meat consumption.

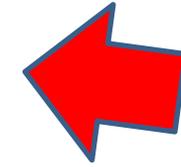


Data source: Food and Agriculture Organization of the United Nations

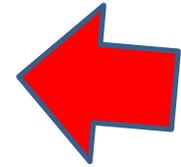
OurWorldInData.org/meat-production | CC BY

- Meat is an important source of nutrition for many people around the world.
- Global demand for meat is growing: over the past 50 years, meat production has more than tripled.
- Challenge: produce and consume meat, dairy and other protein products in a way that reduces its environmental impacts

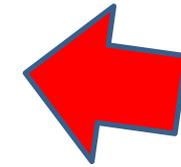
Livestock Industry challenges



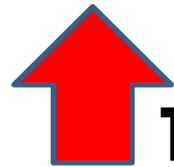
Adverse environmental condition



Lack of new breeding animals



High cost of farm inputs



Transboundary animal diseases



What is BIOTECHNOLOGY?

Biotechnology is the use of biology to develop new products, methods and organisms intended to improve human health and society.

Source:

<https://www.techtarget.com/whatis/definition/biotechnology#:~:text=Biotechnology%20is%20the%20use%20of,and%20the%20discovery%20of%20fermentation.>



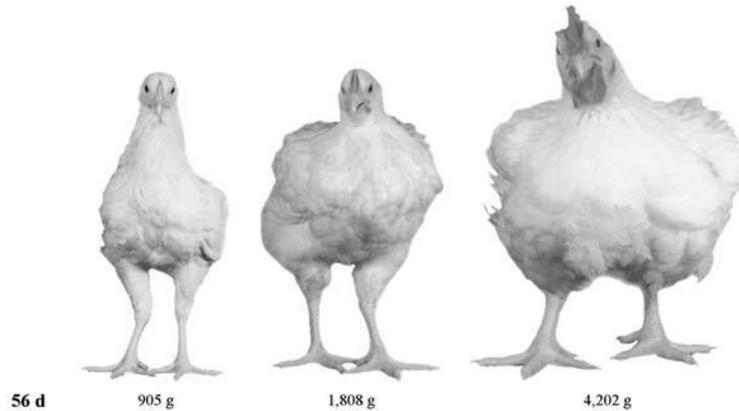
ANIMAL / LIVESTOCK BIOTECHNOLOGY

Has a long history, beginning as far as 8,000 years ago



Traditional Animal Biotechnology

Selective Breeding



What differences can you see?

Domestication and
Artificial Selection



**Modern Animal Biotechnology began only following
discovery of genetic code**



ANIMAL / LIVESTOCK BIOTECHNOLOGY



**Climate Change
and Disease
Resilient or
Resistant
Animals**

**Increased
Income for
Livestock Food
Producers**



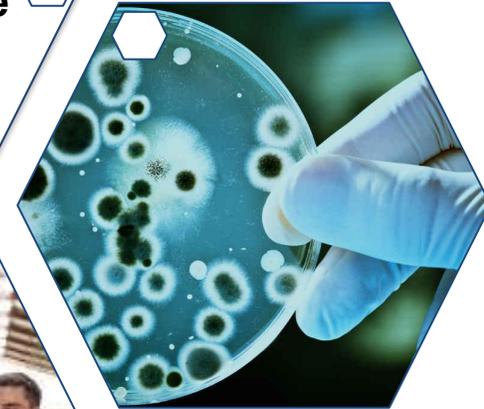
**Doubling Food
Production to
meet the supply
for demand**

**Proper Animal
management**

**Rapid
Diagnosis and
Modern Disease
Surveillance**



**Increased
Income for
Livestock Food
Producers**



The *Cartagena Protocol on Biosafety to the Convention on Biological Diversity* is an international treaty governing the movements of living modified organisms (LMOs) resulting from modern biotechnology from one country to another. It was adopted on 29 January 2000 as a supplementary agreement to the Convention on Biological Diversity and entered into force on 11 September 2003.

(Cartagena, Colombia to Montreal, Canada)



CARTAGENA PROTOCOL

Article 3 – Use of Terms

(g) "Living modified organism" means any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology;

(h) "Living organism" means any biological entity capable of transferring or replicating genetic material, including sterile organisms, viruses and viroids;

(i) "Modern biotechnology" means the application of:

- a. In vitro nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles, or
- b. Fusion of cells beyond the taxonomic family,

that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection;

Introduction of Genetically Modified (GM) Animals

- **GM Animal** - involves altering its genetic material by adding, changing or removing certain DNA sequences in a way that does not occur naturally. It aims to modify specific characteristics of an animal or introduce a new trait, such as disease resistance or enhanced growth (EFSA).
- Two Methods:
 - Transgenesis / Cisgenesis (transfer of genes) in animals
 - Deletion of genetic information

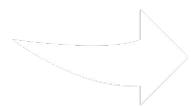
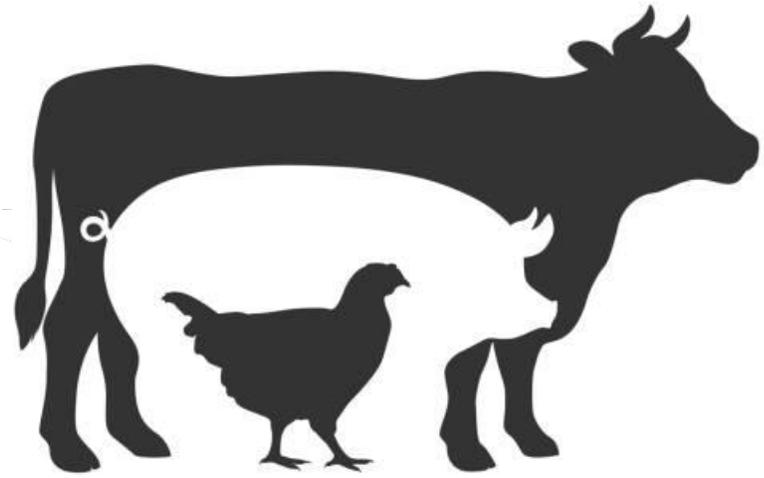




INPUTS

- Disease Models / Resistance
- Xenotransplantation
 - Cells
 - Tissues
- Organs
- Bio Pharmacology
 - Drugs
 - Devices
 - Biologicals
- High Value Products

- Milk and meat quality
- Milk and meat composition
- Productivity increased
- Conformation
- Robustness
- Fecundity
- Environmental Resilience
- Environmental Footprint

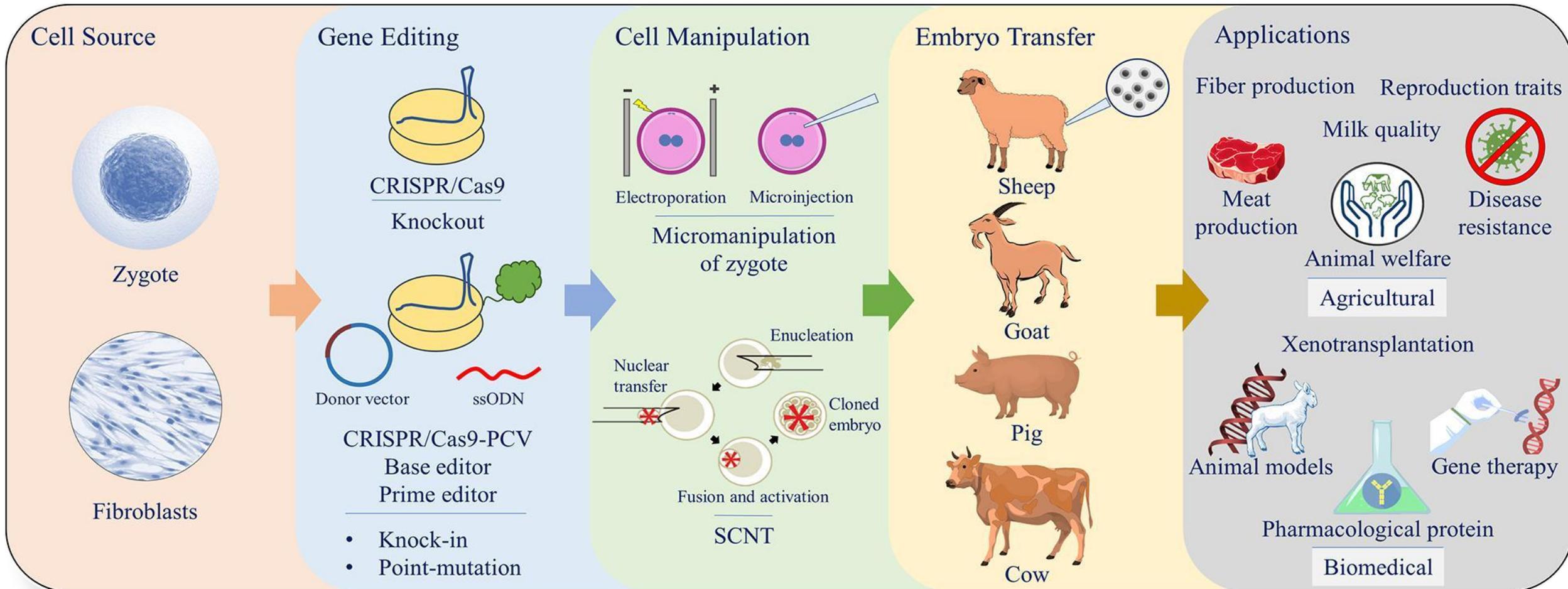


OUTPUTS



Use of New Breeding Innovation as a *Driver for Change* in Livestock

Cell Mediated Genomic Editing

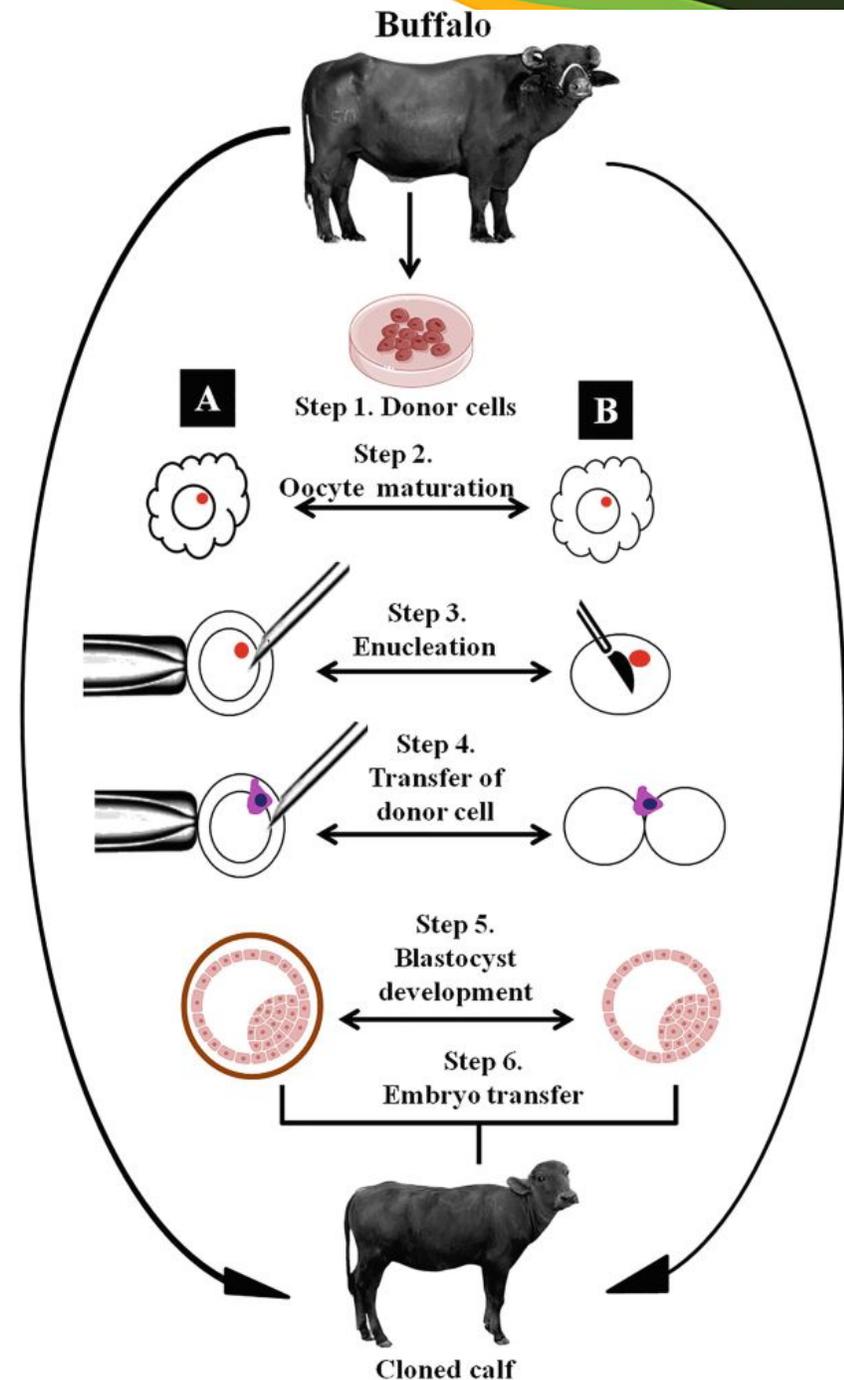


The Philippine Carabao Center has adopted the **SOMATIC CELL NUCLEAR TRANSFER** technology to complement other existing reproductive tools for buffaloes. The present work was conducted to develop/optimize a system for cloning through somatic cell nuclear transfer in water buffalo. Buffalo clone embryos had been successfully produced *in-vitro*.



The Philippine Carabao Center is steadily moving toward its target of improving the genetic traits of Philippine carabaos to produce better sires. Through its Carabao Development Program, thousands of dairy farmers in the Philippines have availed of and utilized the technologies in artificial insemination and the use of riverine bulls for natural mating to produce quality crossbreds.

Micromanipulators-based SCNT



Micromanipulators-free SCNT, called handmade cloning (HMC)

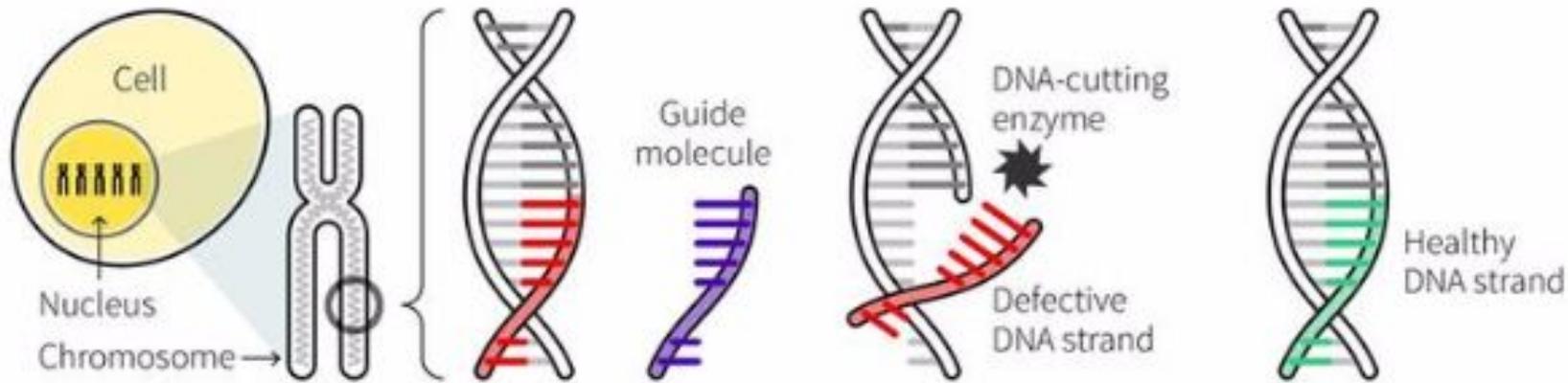


Gene Editing

DNA editing

A DNA editing technique, called CRISPR/Cas9, works like a biological version of a word-processing programme's "find and replace" function.

HOW THE TECHNIQUE WORKS



A cell is transfected with an enzyme complex containing:

- Guide molecule
- Healthy DNA copy
- DNA-cutting enzyme

A specially designed synthetic guide molecule finds the target DNA strand.

An enzyme cuts off the target DNA strand.

The defective DNA strand is replaced with a healthy copy.

Sources: Reuters; Nature; Massachusetts Institute of Technology



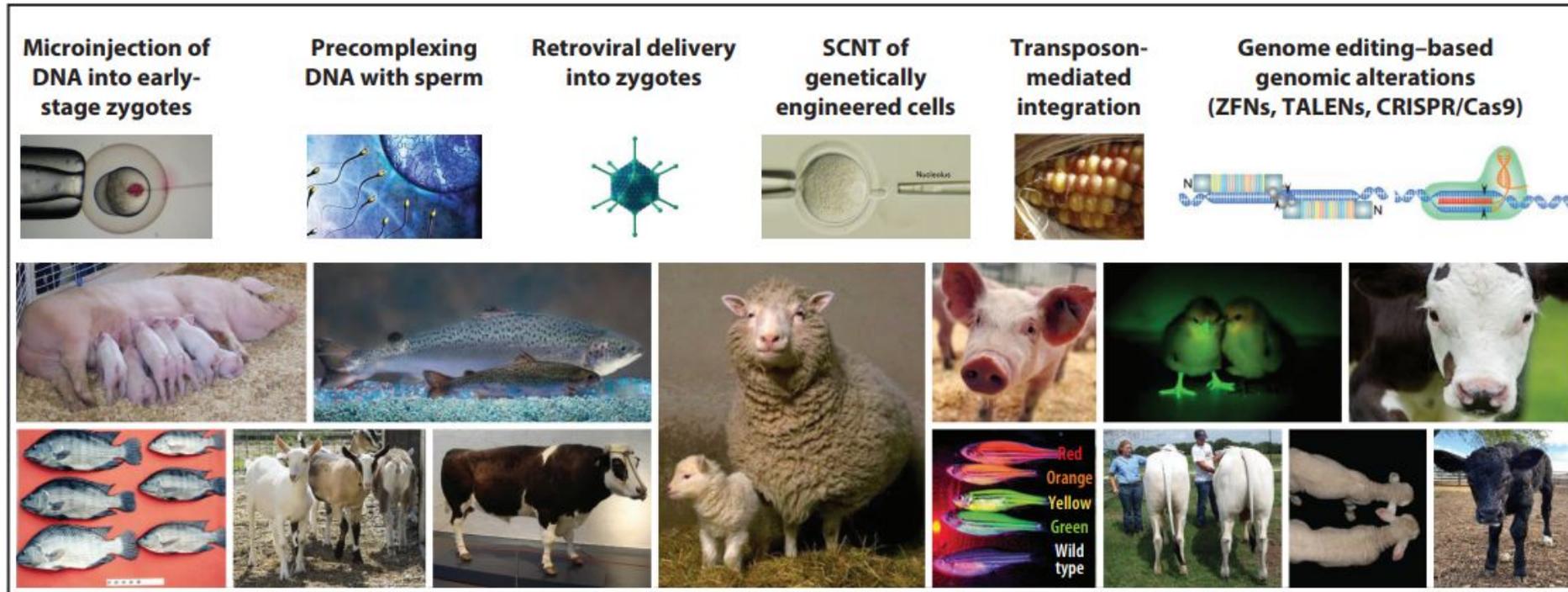
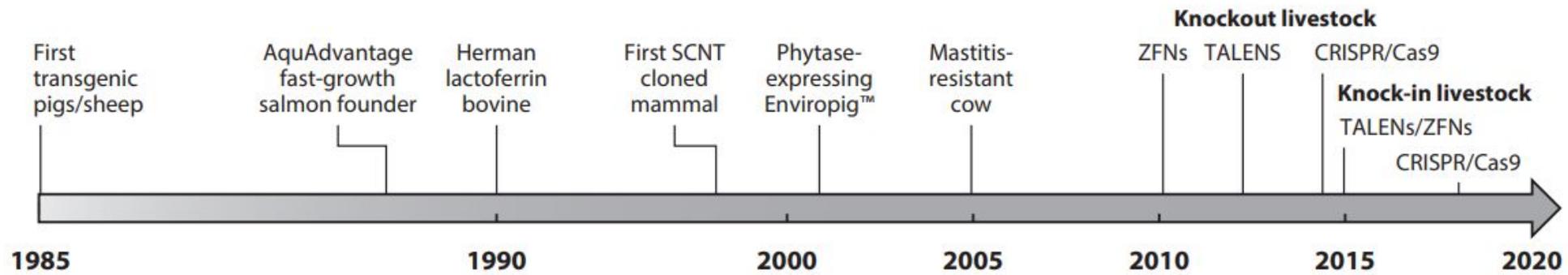


Figure 1

An abbreviated schematic history of 35 years of genetically engineered livestock featuring some of the well-known celebrities of the field. Abbreviations: CRISPR/Cas9, clustered regularly interspaced short palindromic repeat targeted by Cas 9 nuclease; SCNT, somatic cell nuclear transfer; TALEN, transcription activator-like effector nuclease; ZFN, zinc-finger nuclease.



Gene Edited Animals in the Pipeline



Littlejohn et al., *Nature Communications* 5: 5861 (2014)

- Intentional Genomic Alteration
- Slick hair coat – to better regulate their internal body temperature with an increased capacity of sweating

Source: ISAAA Inc., 2021



PMEL -/-

PMEL +/-

- Color diluted dairy cattle
- Lightening the coat color can reduce the radiative heat gain from exposure to the sun

Source: Goetz Laible, 2022

Gene Edited Animals in the Pipeline



- A typical horned dairy cow (right) and a genome-edited cow without horns that contains a DNA sequence found in hornless cattle (Photo courtesy of Alison L. Van Eenennaam, Dept. of Animal Science, University of California-Davis)

Source: ISAAA Inc., 2021



- GalSafe Pigs
- GM pig to prevent allergies

Source: Goetz Laible, 2022



Gene Edited Animals in the Pipeline

B2R Woodhill Complete A130-C2

Black to Red



- Red Angus
- Red Angus females have excellent milk production and have a strong maternal instinct
- This breed produces a highly desired carcass with the meat being of excellent quality, this is due to the intra muscular marbling

Source: Goetz Laible, 2022



Gene Edited Animals in the Pipeline



- Porcine Reproductive and Respiratory Syndrome -resistant pigs

Source:

<https://www.ed.ac.uk/roslin/facilities-resources/larif/case-studies/industry-partners>



- Bird flu resistant chicken
- contain an extra gene that interrupts the transmission of bird flu

Source:

<https://www.ed.ac.uk/roslin/news-events/latest-news/archive/2019/gene-edited-chicken-cells-resist-bird-flu-virus>

Gene Edited Animals in the Pipeline



Photograph: INTA (National Agricultural Technology Institute Argentina)

- Rosita Isa – was born that expressed milk containing proteins present in human milk but lacking in cow milk.

Source:

<https://www.theguardian.com/environment/2018/jun/24/genetically-engineered-animals-the-five-controversial-science>



- A genetically modified male mosquitoes that carry a “self-limiting gene”; the offspring do not reach adulthood, reducing the spread of mosquito-borne diseases (Oxitec)

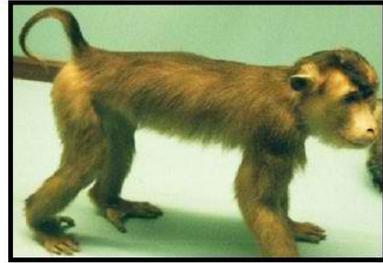
Applications and uses of GM / GE Animals

DISEASE

Nonhuman primate models for AIDS



Macaca mulatta (rhesus)
Macaca nemestrina (pigtailed)
Macaca fascicularis (crab-eating)

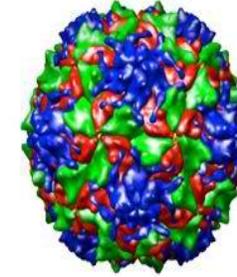


- HIV-1: only replicates in chimpanzees--disease in 10 years
- SIV: simian immunodeficiency virus; transferred from African to Asian macaques in captivity and caused disease like AIDS
- SHIV: chimera that has the HIV Envelope and the backbone of SIV; these viruses cause disease after passage in macaques

Nancy L. Haigwood
Seattle Biomedical Research Institute

TEST SYSTEM DEVELOPMENT

Transgenic mice have been invaluable tools:



An example:

Normal mice cannot be infected with polio virus. They lack the cell-surface molecule that, in humans, serves as the receptor for the virus. So normal mice cannot serve as an inexpensive, easily-manipulated model for studying the disease. However, transgenic mice expressing the human gene for the polio virus receptor

- * can be infected by polio virus and even
- * develop paralysis and other pathological changes characteristic of the disease in humans.

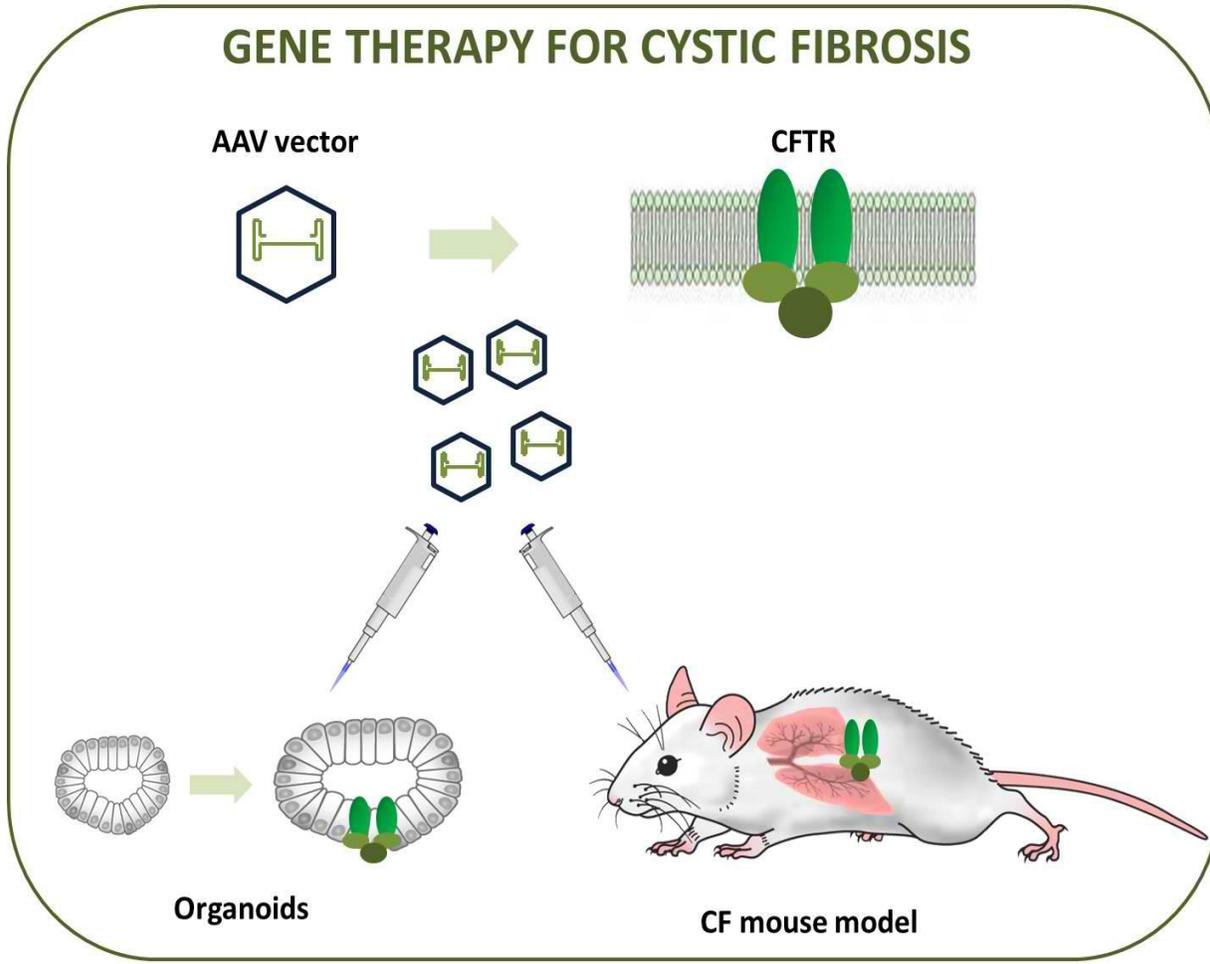
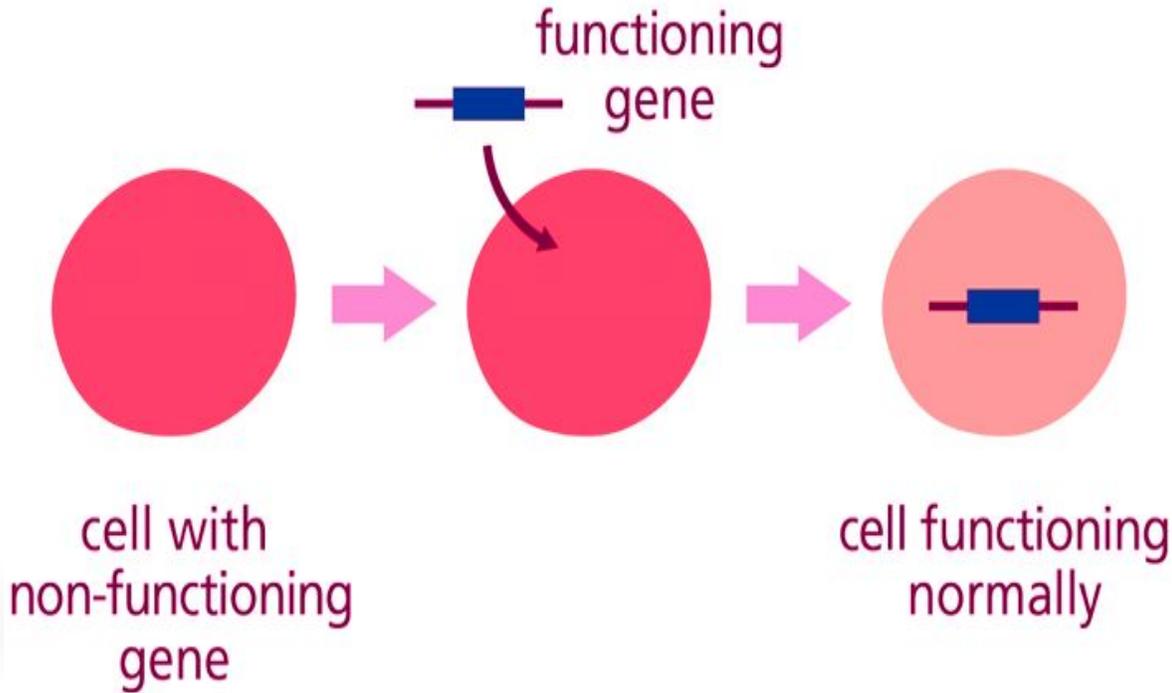
- Work is in progress to develop new models by altering the susceptibility of mice to pathogens of humans.



Applications and uses of GM / GE Animals

GENE THERAPY

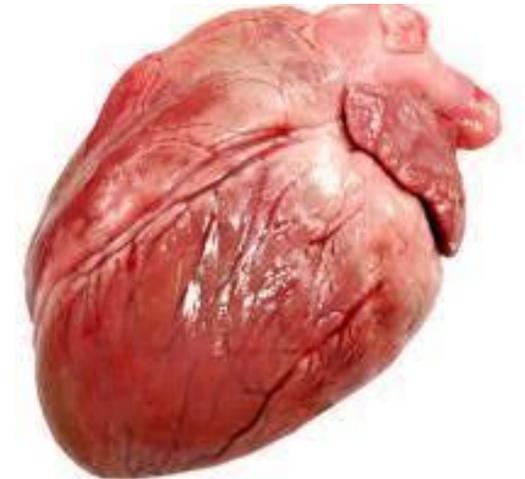
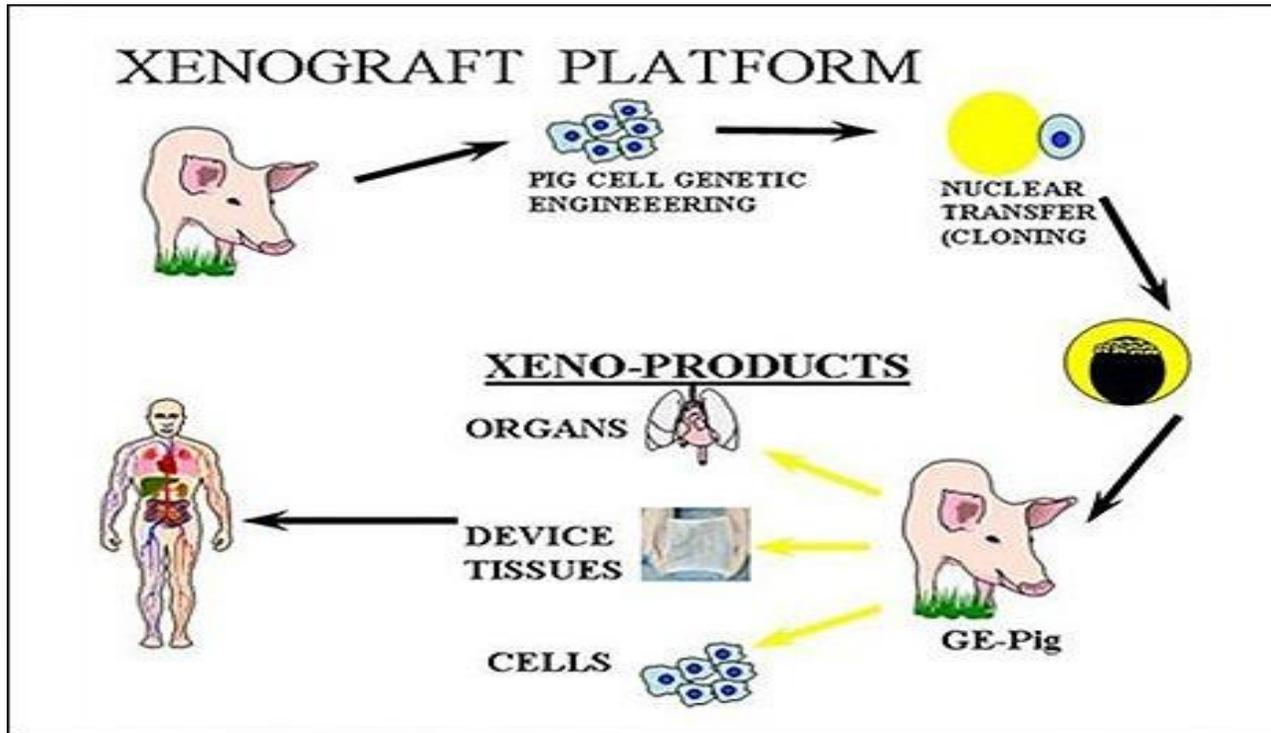
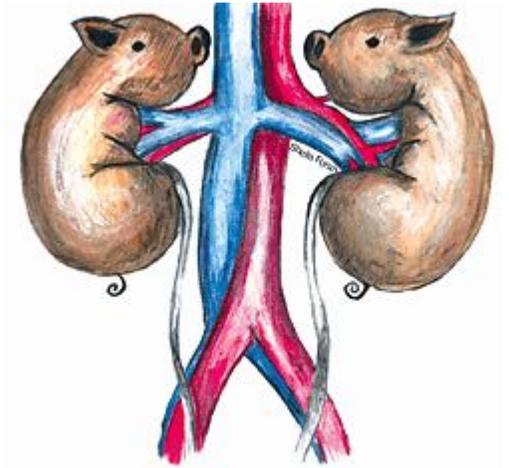
Gene Therapy



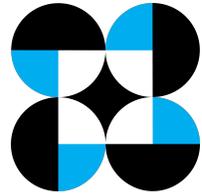
Applications and uses of GM / GE Animals

XENOTRANSPLANTATION

Larger species, such as pigs and baboons, are preferred for development as donors because of the similarity of their organ size to that of humans.



GM Animals Regulatory Policy



DOST-DA-DENR-DOH-DILG
Joint Department Circular
No. ____, Series of 2022

Subject: Rules and Regulations for the Research and Development, Handling and Use, Transboundary Movement, Release into the Environment, and Management of Genetically-Modified Animal and Animal Products Derived from the Use of Modern Biotechnology



STATUS: Under series of Stakeholder Consultation within the country

GM Animals Regulatory Policy

Applicability

- genetically-modified fisheries and other aquatic resources
- domesticated animals and biological products used for animal husbandry or veterinary purposes
- biological agents used for biocontrol derived from the use of modern biotechnology and containing novel combinations of genetic materials

Products of gene editing that do not contain novel combinations of genetic materials are not covered by this Circular.



Ways Forward

To ensure an enabling environment for biotechnology undertakings:

1. Implementation of a clear, predictable, science-based, and risk-proportionate regulations
2. Establishment of an adaptive and responsive policies that can adapt to rapid advancements and emerging technologies
3. Foster international cooperation and harmonization of regulatory standards to streamline global biotech development and facilitate cross-border research and trade
4. Adequate/sufficient funding for biotech, research, and innovation
5. Education and Public Awareness



Thank you!

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