POLICY BRIEF

Modern Animal Biotechnology:
Benefits, Future Directions, and Policy Recommendations

Ernelea P. Cao, PhD
Professor, Institute of Biology, College of Science, University of the Philippines, Diliman, Quezon City, Philippines

Policy Recommendations

- A science-based regulatory framework that is specific for GM animals should be in place in anticipation of applications for entry of products to the Philippines. A separate assessment process should be established for genome-edited animals.
- Continuous and effective science communication among researchers in public and private institutions, government regulatory agencies, and consumers, with an emphasis on the responsible use of biotechnology, is needed to reap the benefits of innovative animal technologies.

Introduction

The domestication of important livestock animals is said to have occurred in sedentary communities which were engaged in early agriculture (Cucchi and Arbuckle, 2021). As early as 10,500 to 10,000 BC, sheep, goats, pigs, and cattle were domesticated (Colledge et al., 2013). The earliest type of animal biotechnology for the improvement of strains involved breeding, especially in livestock and fish. The English farmer, Robert Bakewell (1725-1795), was the first to apply sheep and cattle breeding successfully for the improvement of the wool and meat quality, by methodical selection and inbreeding, respectively. (Wood, 1973). Since then, various breeding activities have been done, for example, in dairy cattle for the improvement of their milk production, protein composition, fertility, longevity, and mastitis resistance.

In the Philippines, the Philippine Carabao Center (PCC) leads in the improvement of the genetic potential of water buffalo for milk and meat production, to meet the needs of the growing Filipino population. This is done through the introduction of the riverine buffalo germplasm into pre-identified populations of swamp buffaloes (PCC, n.d.)

Developments in Modern Biotechnology in Animals and their Benefits

With the discovery of molecular techniques in biology, modern animal biotechnology was born. The establishment of the Molecular Genetics Laboratory of the PCC in 2008 facilitated the use of various techniques to select superior animals for breeding, including DNA fingerprinting and molecular marker technologies for characterization, genetic resource conservation, and improvement of the water buffaloes.

Compared to conventional breeding and selection, genetic engineering or recombinant DNA technology allowed for the faster and more specific introduction of genes that control economically-important traits in animals. This gene technology was developed with the discovery of enzymes called restriction endonucleases that can recognize and cut the DNA of a host organism at precise locations. It allows for the introduction of foreign DNA, which codes for the expression of favorable traits in the genetically modified (GM) or genetically engineered (GE) organism. It was used to produce animals to increase food production, stop the spread of diseases, and even remediate environmental pollution. Modern

animal biotechnology is also applied to produce therapeutic compounds such as hormones, growth factors, antibodies, and vaccines.

Genetically Engineered Animals

The most reported GE animals and their uses (ISAAA, 2017) are the following:

GE Fish (GE Salmon)

As of 2022, the only commercialized GE fish is the GE salmon, trademarked as AquAdvantage™ salmon, which was developed to increase food production. This was introduced by AquaBounty Technologies after almost three decades of development. It is an Atlantic salmon that grows twice the size of the non-GE salmon for the same growing period because it contains a growth hormone gene from the Pacific Chinook salmon with a promoter sequence from the ocean pout. This variety of salmon was also approved by the US Food and Drug Administration (US-FDA) in 2015 since it was assessed to be safe as food and there were no biologically relevant differences as compared with the non-GE Atlantic salmon. The biotech salmon is available in the USA and Canadian markets.

GM Insect (GM Mosquito)

Many diseases like Malaria, Dengue fever, Zika, and Chikungunya have mosquitoes as vectors, particularly, through the females that bite their prey. To avert the spread of such diseases through the mosquito vector, genetic engineering was used to reduce the female population through an enzyme called I-Ppol that cut specifically within the mosquito's ribosomal gene sequences. A transgenic strain that expressed the I-Ppol enzyme in sperm cells was developed so that their X chromosome would be cleaved and the mosquitoes will produce mostly Y chromosome-bearing sperm cells that will eventually produce only male offspring. In the case of the males developed as the Oxitec Friendly™ Aedes mosquitoes, they contain a gene that kills the progenies at the larval stage. When they breed with the wild female population, they produce non-viable larvae that die before adulthood. It was reported that there was a 91% reduction in Dengue fever cases in the CECAP/El Dorado District of Brazil in 2016. Likewise, the Aedes mosquitoes were also reported to avert the spread of the Zika virus in Brazil that causes microcephaly in children.

GM Pig (Enviropig)

The Enviropig™ has been genetically modified to contain the gene that produces the phytase enzyme in their salivary glands, which degrades the indigestible phytate in the feed. Pigs release a significant amount of phosphorus in their manure from the feeds they eat, which leach from the piggery farms into the groundwater that causes algal blooms and cause pollution in freshwater systems. This was already submitted for regulatory review in the US and Canada in 2007 and 2009, respectively.

GM Fish (GloFish)

GloFish™ or the glowing fish was made to detect pollution and not for consumption. Bioluminescence is a naturally occurring phenomenon. The GloFish was developed by inserting a naturally-derived fluorescence gene to the fish to determine polluted water systems. It has also been commercialized as a home aquarium pet in 2003 under the license of Yorktown Technologies. There are 12 lines of GloFish™ in the market that have taken up a significant percentage of sales in the aquarium fish industry.

GE Chicken (Bird-flu Resistant Chicken)

This transgenic chicken has resistance to the bird flu (Influenza) through a short-hairpin RNA that works as a decoy that inhibits and blocks the spread of the Influenza virus. The subsequent tests showed that transmission of the virus to both transgenic and non-transgenic fowl was prevented. This technology is then a potential measure to prevent the continuing threat of bird flu in poultry production that also threatens human health.

With new discoveries in molecular genetics such as genome editing, more applications have been discovered to produce more food at an even easier and faster pace. Genome editing involves the modification of the genetic information in an organism by silencing, deleting, or modifying particular DNA sequences to prevent or allow the expression of certain traits. The most used techniques in genome editing are the clustered regularly interspaced short palindromic repeats (CRISPR)-CRISPR-associated protein 9 (Cas9), transcription activator-like effector nucleases (TALENs), zinc-finger nucleases (ZFNs), and homing endonucleases or meganucleases.

Research on Genome-edited Animals

While a lot of genome-edited animals are in the research stage compared to genome-edited plants, some promising studies are the following (Tait-Burkard et al., 2018):

Dehorned Cattle

Dehorning has been practiced by many dairy farmers and handlers to achieve reduced risk of injury from the horns, reduced competition for feeding trough space, and fewer aggressive behaviors among animals. Routine dehorning poses an animal welfare concern due to the pain and the potential for injury inflicted during the procedure. However, there are naturally-occurring hornless cattle, called "polled," particularly in beef cattle rather than in dairy cattle. TALENs was used to introduce the Pc POLLED allele into the genome of bovine embryo fibroblasts from four lines of cattle.

Animals with Edited *Myostatin* Gene

Muscle growth is an important characteristic considered for farmed animals for increased food production. The myostatin (also known as growth differentiation factor 8 or GDF8) gene has been edited to be underactive in cattle, sheep, goat, and channel catfish to increase muscle growth.

Disease-resistant Animals

In pigs, the reproductive and respiratory syndrome has been an infectious disease of concern. A single locus on the pig chromosome 4 (GBP5, encoding guanylate-binding protein 5) has been targeted to produce resistant pigs. African swine fever is another disease of concern. Researches are being conducted to study the variation in the RELA (a component of the NF-κB transcription factor known to play a role in stress and immune responses) gene between resistant and susceptible pigs.

Sterile Farmed Atlantic Salmon

Sterility has also been a target in farmed Atlantic salmon, to avoid escapees interbreeding with wild stocks or populations. Genome-editing approaches have also been successfully applied to the dead-end protein, which is encoded by the dnd gene, to induce sterility.

Conclusions and Future Directions

A lot of progress has been achieved in the development of GM animals that will reap benefits in terms of increased food production, disease prevention, and even environmental remediation, as indicated in the aforementioned examples. With global trade, the introduction of GM animals will not be farfetched, and the Philippines should be ready to handle applications for entry of such biotech animals, including their products. Just like the experience of the country in the introduction of genetically modified crops, a science-based assessment method was all that was needed for our regulatory agencies to be able to evaluate the safety of GM crops being applied for direct use as food/feed and for processing or for propagation to be able to avail of their benefits, particularly, in food production. This science-based assessment approach should also be done for GM animals as well as genome-edited animals. However, the assessment method for genome-edited animals should be different. Compared to GM technology, most genome-edited animals do not have a foreign DNA sequence or transgenes in the final product. Such a technique renders more acceptability among consumers.

Since 2002, the Philippines has been regarded as the leader of biotechnology in Southeast Asia – being the first country in the region to implement a regulatory framework on GE crops and approve cultivation for food and feed. Its current regulatory system governing the use of modern plant biotechnology is overseen by five departments: science and technology (DOST), agriculture (DA), environment and natural resources (DENR), health (DOH), and the interior and local government (DILG) through a Joint Department Circular (JDC). In 2022, this JDC was revised to address bureaucratic delays that were not consistent with the passage of Republic Act No. 11032 or the Ease of Doing Business and Efficient Government Service Delivery Act of 2018. These developments in crop biotechnology regulation can be the pattern for setting up a robust regulatory framework for biotech animals.

Since developments and improvements in modern animal biotechnology are in progress and are expected to come up with products for commercialization soon, effective science communication among researchers in public and private institutions, government regulatory agencies, and consumers should continue. With an emphasis on the responsible use of biotechnology, which the Philippine government espouses, a consensus on the best possible approach is needed in order to reap the benefits of these new technologies.

Ernelea P. Cao, PhD, Professor, Institute of Biology, College of Science, University of the Philippines, Diliman, Quezon City, Philippines

References

ISAAA. 2017. Pocket K No. 55 Biotech -improved Animals. Retrieved October 15, 2022, from https://www.isaaa.org/resources/publications/pocketk/55/default.asp

Colledge, S., J. Conolly, K. Dobney, K. Manning, and S. Shennan. 2013. Origins and Spread of Domestic Animals in Southwest Asia and Europe. Publications of the Institute of Archaeology, University College London. Walnut Creek, CA: Left Coast Press.

Cucchi, T. and B. Arbuckle. 2021. Animal Domestication: From Distant Past to Current Development and Issues. Animal Frontiers 11(3):6-9. https://doi.org/10.1093/af/vfab013

Department of Agriculture - Biotechnology Program. n.d. 2002. Department of Agriculture Administrative Order No. 8 (DA AO No. 8), Series of 2002. Retrieved October 14, 2022, from http://biotech.da.gov.ph/upload/DA_AO_8-signed_copy.pdf

Department of Science and Technology - National Committee on Biosafety of the Philippines. n.d. DOST-DA-DENR-DOH-DILG Joint Department Circular No.1, Series of 2016, Subject: Rules and Regulations for the Research and Development, Handling and Use, Transboundary Movement, Release into the Environment, and Management of Genetically-Modified Plant and Plant Products Derived from the Use of Modern Biotechnology. Retrieved October 15, 2022, from https://ncbp.dost.gov.ph/21-joint-department-circular

Philippine Carabao Center. n.d. Genetic Improvement. Retrieved October 15, 2022, from https://www.pcc.gov.ph/genetic-improvement/

Official Gazette of the Philippines. 2018. Republic Act 11032. Signed 2018. Retrieved October 15, 2022, from https://www.officialgazette.gov.ph/2018/05/28/republic-act-no-11032/

Tait-Burkard, C., Doeschl-Wilson, A., McGrew, M.J., Archibald, A. L., Sang, H. M., Houston, R. D., Bruce Whitelaw, C., and M. Watson. 2018. Livestock 2.0 – Genome Editing for Fitter, Healthier, and More Productive Farmed Animals. Genome Biology 19, 204. https://doi.org/10.1186/s13059-018-1583-1

Wood RJ. 1973. Robert Bakewell (1725-1795), Pioneer Animal Breeder, and His Influence on Charles Darwin. Folia Mendeliana 58:231-242. PMID: 11634455.

Philippine Agriculture and Fisheries Biotechnology Program
2nd Floor DA BSWM Building, Elliptical Road cor. Visayas Ave.
Diliman, Quezon City
Philippines
https://biotech.da.gov.ph

International Service for the Acquisition of Agri-biotech Applications (ISAAA) Inc.
3rd Floor, Khush Hall, International Rice Research Institute
Los Baños, Laguna
4030 Philippines
https://www.isaaa.org

Southeast Asian Regional Center for Graduate Study and Research in Agriculture (SEARCA)
College, Los Baños, Laguna
4031 Philippines
https://www.searca.org

(February 2023)

Ernelea P. Cao, PhD, Professor, Institute of Biology, College of Science, University of the Philippines, Diliman, Quezon City, Philippines