Animals in Research: Transgenic animals

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The use of animals in research is a very controversial yet important topic to New Zealand. Animals are widely used across different factions of science such as cancer testing, cosmetic use and agricultural advancement. Animals used for experiments in New Zealand are often used in agricultural research. In this report I will be focusing on issues surrounding the use of cows in agricultural research conducted within New Zealand. The topic consists of the use of genetic engineering to make transgenic cows and their contribution to economic success.

In 2016, over 100,000 cows were used for veterinary and biomedical research. Some animals are experimented on in an attempt to increase the milk yield for the agricultural industry. The scientists in AgResearch New Zealand successfully genetically engineered cows to produce up to 70% more milk than normal cows; these are referred to as transgenic cows and they have an extra gene(s) inserted into their DNA. The inserted gene (transgene) may originate from the same species or from an entirely different species. The transgene is present in every cell of the cow's body however, it is only fully expressed in the mammary glands. This also means that whatever protein made by the transgene (as only one gene codes for one protein) will only be found in the milk and cannot be extracted from elsewhere.

However, the insertion of the transgene is only successful if it is inherited by its offspring. The success rate for transgenesis is very low. Animal internal structures are quite large and much more complex, making them more susceptible to environmental factors therefore manipulation of genes is significantly harder. When editing the genes of a cow, the transgene must be inserted through the germ line of a cell. This way every cell of the offspring will contain the same revised genes. Germ cells control transferring an organism's genes to its offspring. Right now there are several ways to modify the genome of a cow such as Recombinant Retroviruses, Pronuclear Injection, Sperm-Mediated DNA Transfer, Embryonic Stem Cells, Germ Cell Transplantation and Nuclear Transfer "Cloning". The main ways to modify are DNA microinjection and Retrovirus-mediated gene transfer.

DNA microinjection is when the desired gene(s) from another species or an organism from the same species is injected into the nucleus of a germ cell. These modified cells will first be examined as it develops in a lab and then transferred to a cow once it passes the specific embryo state. This form of gene transfers and modification is predominantly used in transgenic farm animals and for agricultural industry success. However, due to reproduction processes being random, the transgenic cows are mated often to ensure that there are enough transgenic offspring. However Individually mating these cows has a very low success rate and can be a waste of time and resources.

Retrovirus-mediated gene transfers result in an organism known as a chimera; an animal with DNA comprising 2 or more animals. Retroviruses are viruses that carry their genetic material in the form of RNA instead of DNA. These retroviruses are used as vectors to carry the transgene into the organism's cell which will result in an organism that consists of tissues/cells of diverse genetic constitution, which is a chimera. A vector in molecular biology means a DNA molecule used a vehicle to transfer foreign genes (in this case a transgene) for it to be expressed in the organism, also more commonly referred to as recombinant DNA. In 1974, mice were again the first successful experiments when the simian virus was used and inserted into the mice embryo, resulting in the mice having and expressing DNA given. Transgenic cows made from Retrovirus-mediated gene transfer will be inbred for a long time until they get offspring that are homozygous for the transgene and its phenotype.

These advancements in animal biotechnology provide many opportunities to improve health and the environment. The benefits of production of transgenic animals is that they produce milk of higher nutrient and mineral content with a higher milk yield. The main nutrients in milk include protein, fat, and lactose. By elevating any of these nutrients we can significantly improve the growth and health of their offspring. Human health is directly impacted by the change in milk composition as humans also consume cow milk. By changing or adding a transgene then you are changing or adding one protein to the composition (as one gene codes for one protein). Transgenic animals may soon be used in medical applications. Patients may be able to get

organs from transgenic animals or at cellular level get proteins from animals. As the human body would reject foreign organs from non-transgenic animals, transgenic animals are a different case. For example, xenotransplantation is disadvantaged by using pig proteins that can cause the human body to reject them but research is proceeding to interchange this protein with a human protein. Milk-producing transgenic animals are particularly useful for medicinal research and development. Treatments for illnesses such as hereditary emphysema, phenylketonuria and cystic fibrosis further research is being conducted in the production of milk using transgenesis as a solution.

Some social implications that may arise from the genetic modification of farm animals are in relation to the risks and opportunities for the NZ economy and ethical issues around the matter. In general the biomedical use of transgenic animals is more accepted by the New Zealand public than the agricultural use of transgenic animals. Some members of the public may consider the use of animals in research and especially transgenic cows to be very immoral, that animals should have the same rights as us. People/groups that are against commercial use of animals will be most likely against the idea of transgenesis. NZ economy may also be affected by using genetic modification and transgenesis, overseas buyers may lose interest in the New Zealand agricultural industry due to personal ethics they might uphold. For the same reasons New Zealand may lose access to the overseas market for the export of products. The New Zealand economy is very dependent on the production and environmental characteristics of animals. Transgenesis may provide a chance to evolve these characteristics and create new products to sell and new subdivisions in the NZ economy.

Ngati Wairere and GE Free are against the use of animals for genetic modification and agricultural use. Claire Bleakley, president of GE Free New Zealand has said that "The report is a catalogue of disasters. AgResearch has constantly said that there is no problem, and that the animals suffer from basically normal farming disorders. When you look at this, these animals are suffering inordinately - from sterility, from chronic illness, from sudden death". Bleakly had expressed her concerns about the covering up of possible extreme suffering and deformities caused to the cows undergoing transgenesis. She believes that this matter directly affects New Zealand's stance on the ethics and morals and how we are portrayed globally. Bleakly has made speculations that illnesses and deformities were caused by the insertion of foreign DNA into the embryos. Ngati Wairere have guardianship over the land that is occupied by AgResearch. Ngati Wairere's opposition to research relates to the placing of copies of human genes into cows in order to produce a human-cow hybrid, or transgenic cow. Ngati Wairere is concerned with the fact that these experiments will significantly influence genealogy and the flow of nature; Transgenesis does not align with Maori teachings within the Ngati Wairere.

As stated by Dr Tony Conner (Science Group Leader at AgResearch NZ), "The genetic technologies are developing at such a pace internationally that it's important we don't get left behind". Connor explains that if we aren't quick to develop our genetic modifications to the agriculture industry, our small economy could collapse, whilst other economies prosper. As agriculture is the country's biggest industry, NZ's economy relies on the Agriculture sector (i.e. dairy, meat, wool, etc.). Hence, taking advantage of the positive environmental impacts caused by transgenesis, may boost NZ's economy. Dr David Wells, a principal scientist in the reproductive team at AgResearch has stated that "We acknowledged that there are animal welfare concerns with the current technology - rather the methods we've used to generate those embryos. Many of the deformities that have incurred [are due to] incorrect programming". Wells had acknowledged the risk proposed by Bleakly but had claimed that research was once sided and that AgResearch had done its best to manage the cows by hiring many veterinary units and animal husbandry teams.

In regards to the implications stated in this report the biological implications are evidently more significant than the social implications. This is because the point of transgenesis and genetic modification of animals as a whole is to benefit the said organisms health, their offspring's health and human health. I believe the prospects of having a potential new way to find cures or have better treatments while using animals to experiment on outweighs the ethical issues of causing animals pain and suffering. I believe in the fact that if we genetically engineer cows to produce less lactose and make human protein it will be such a big achievement and advancement to science. If we further develop and solidify gene editing there are endless possibilities to what we can improve. Xenotransplantation will become a more successful technique to help people with diabetes, cystic fibrosis and other diseases which require a change of protein. Changing milk composition to accommodate more human proteins and cater to specific digestive needs of the public is very advantageous to population health of New Zealand. As prior stated, economic consequences can be derived from the environmental implications. In truth, if transgenesis were to be used internationally, NZ not

adopting transgenesis into dairy would in fact hurt our economy greatly. The increased efficiency to agricultural practices that transgenesis would provide (once accuracy and success rates increase), would lead to NZ's Agricultural sector growing tremendously. Ultimately, our GDP would rise, and we'd remain a major financial contender on a global scale. But, as the negative biological implications outweigh the positive social implications, I believe transgenesis on a larger scale should only be put in place after the success rates and proper regulations are put in place.

As explained in my opinion, the need for animals in research and proper regulations is significant, and so my proposed societal action plan is based on just that. Currently, gene editing and transgenesis related laws and regulations are not very clear and decisive. The lack of clear legislation could lead to incorrect applications of transgenesis. To prevent this from happening again, and hence alleviate the negative biological impacts, the NZ government should hold a national referendum so that members of the public can vote for/against the implementation of transgenesis specific regulation laws in regards to the use of animals in research. As a democratic country, it is extremely important that all citizens that are of voting age have a say in the country's future. If this goes positively then New Zealand will have an improved dairy industry and improved medicine. By doing this we might see a future decrease in allergies and lactose intolerant rates in New Zealand. We might also see enhanced animal welfare and health which will benefit farmers and the wellbeing of animal rights activists. I think the prospects of having a potential new way to find cures or have better treatments while using animals to experiment on outweighs the ethical issues of causing animals pain and suffering. People not caring about this referendum might prove to be a potential issue. Since the government isn't legally forced to oblige to the outcome of the referendum. But the conduction of the referendum may bring forth some changes in the New Zealand laws surrounding the use of animals in research and transgenesis, whether they shut down the research or restrict it or increase funding and support it.

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