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Present status of genetically modified animal products: A minireview

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Abstract
The production of Genetically modified organisms (GMOs) is one revolutionary biotechnology tool. GMO has integrated a gene or DNA sequence which has been transferred by human intervention, into the genome of a cell. GMOs are living beings that have had their genetic code changed in some way and are able to pass the modification on to its offspring. GMOs have wide applications and play important roles in biomedical research, providing better nutrition, enhancing human health, livestock production, research and much more. Gene transfer is a comparatively rapid way of altering the genome of domestic livestock. Animals are engineered with special attention on their fast growth, better health and disease resistance. Researchers are able to review the mechanism of the human disease and their possible cures. Purpose of conservation of endangered can be also fulfilled with the technique. Development of GMOs will provide a scope in direct genetic manipulation of livestock. Such effective means of increasing food production are needed with the increasing population and changing climate conditions. Controversies are also associated with the production of GMOs however, if GMOs can be shown to be both healthful and safe, consumer resistance to these products will most likely diminish. The use of these tools will have a great positive impact benefitting mankind in a timely and more cost-effective manner.

Keywords: genetically modified organisms, DNA, livestock

Introduction
Genetically Modified Organisms (GMO) are exploited in many fields of science and industry like medicine, livestock production, research, conservation etc., for the human needs. There is an immense number of applications one can consider by manipulating the genetic material of the animals, but it should be in line with numerous ethical considerations. The commercial availability of GMO products is usually questionable. Few efforts have been made lately after many controversial debates, but major work in GMO is evidence of concept studies. Evidence of concept studies describes that the desired genetic change has been attained. The applications of GM animals and their products dwell in various fields.

Livestock
Livestock is mutated with the aim of improvement in economically important traits like milk composition, quality of meat, rate of growth, survival and disease resistance. Animals are engineered with special attention on their fast growth, better health and disease resistance. Certain mutations have improved the production of sheep wool and udder health of cows [1]. Goats are genetically contrived for milk production with strong spider web-like silk proteins in their milk. This silk can be used to create Biosteel, a web-like material [2]. The goat gene sequence has been readjusted to code for the enzyme lysozyme. Researchers wanted to switch the goat milk, to hold lysozyme to fight back bacteria causing diarrhoea in pigs and human beings [3]. Enviropig was a genetically modified Yorkshire pig in Canada. Researchers introduced it with the potential to digest plants phosphorus efficiently. The transgenic construct comprised of a promoter within the murine parotid salivary gland and therefore the Escherichia coli phytase gene was introduced into the pig embryo with the help of pronuclear microinjection. This resulted in the pigs producing the enzyme phytase. Phytase helps in breaking down the indigestible phosphorus in Enviropig's salivary gland [4]. Consequently, the pigs excreted 30 to 70% less phosphorus in manure. The lower concentration of phosphorus in surface runoff further reduces algal growth as phosphorus is the limiting nutrient for algae [5]. Algae consume an outsized amount of oxygen due to which excessive growth may result in dead zones for fish.

A pig was engineered through the expression of a roundworm gene to produce omega-3 fatty acids [6]. Herman the Bull, the world's first transgenic bovine was developed in 1990. Scientists micro-injected embryonic cells with the human gene coding for lactoferrin. In 1994, eight calves were born inheriting the lactoferrin gene. Recently, Chinese scientists have created a line of pigs “CRISPR Bacon” by using CRISPR technology. These pigs are engineered with better body heat regulation, leading to about 24% less body fat than typical livestock [7]. Selectively polled GM dairy cow were developed. DNA was taken from the genome of Red Angus cattle whose dominant characteristic is genetic dehorner or the polled gene. It had been inserted into cells taken from “Randy”, an elite Holstein bull. Each of the offspring is going to be just like Randy but without his horns. Further, their offspring should even be hornless [8]. Cows infused with human genes enhance the antibacterial properties of their milk and also reduce susceptibility to mastitis [9]. Use of CRISPR to increase wool and hair length in sheep [10] and goats [11] has also been attempted. Cows with increased resistance to tuberculosis were created by TALEN brought knock-out of SP110 gene [12]. Cows, sheep, goats and pigs are genetically modified to supply a better yield of meat per animal. For this, Muscle hypertrophy is achieved in sheep by using multiplex gene editing through CRISPR/ Cas9 [13]. Moreover, Myostatin knock-out produced double-muscled sheep [14] and goat [15] using CRISPR/Cas9 technology [16]. used TALEN to prompt mutation within the MSTN gene for the production of super-muscly pigs. China generated genetically engineered dairy cows borrowing genes from human beings for milk production that might be equivalent to human breast milk. New Zealand also developed a genetically engineered cow that produced allergy-free milk [17]. Further, a transgenic cow Rosita was generated in Argentina by synthesizing two human genes to supply milk with similar properties as human breast milk [18]. Moreover, till now, meat available for purchase doesn’t come from an animal that has been “genetically modified”. It refers to if the animal was fed with GMO crops. Furthermore, A research was attempted at Charles Stuart University, Australia following the insertion of a green fluorescent protein from jellyfish into the sex chromosome of chickens which might theoretically allow a scanner to spot whether the eggs are male or female at an early stage of incubation. Gene-edited chickens are produced by both CRISPR/Cas9 system [19] and TALEN [20]. It could potentially produce eggs without a particular egg white protein. it might be beneficial to some people that are allergic to white protein.

Fish production

GM fishes are developed with promoters setting off an over-production of growth hormone which has resulted in dramatic growth improvement in several species, including trout, salmon, and tilapia. A salmon has been produced by AquaBounty Technologies taking half the time for maturing as wild salmon [21]. Chinook salmon gene is inserted in Atlantic salmon and known as fish allowing the fish to produce the growth hormones for the entire year as compared to the wild-type fish that produces the hormone for less than a couple of months. Another gene is infused, which is from the eel-like ocean pout acting as an "on" switch for the hormone. Since Pout has antifreeze proteins in their blood, GM salmon survive near-freezing waters without affecting the growth and their development. In 2015, Aqu Advantage salmon was approved for commercial production, sale and consumption by FDA, USA which is the first-ever non-plant GMO food to be commercialized. All the fishes are going to be female and reproductively sterile to stop the inadvertent breeding of genetically modified fish with wild salmon.

Research

Many organisms have been genetically engineered, including mammals, to incorporate green fluorescent protein (GFP) [22]. GFP allow easy visualization and localization of the products of the genetic modification [23]. Fluorescent pigs are produced for the studies related to human organ transplants, regenerating ocular photoreceptor cells [24]. It became possible to seek out therapies for HIV/AIDS and other diseases in Glow in the dark cats (green fluorescence). It's possible through the feline immunodeficiency virus (FIV) which is related to HIV. Medaka and zebrafish are the two species of fish which are most ordinarily engineered because they have rapid development and optically clear chorions, and also the 1-cell embryo is easier to sight and microinject with transgenic DNA. Zebrafish are model organisms for genetics, developmental processes, behaviour, disease mechanisms, regeneration and toxicity testing. Their transparency allows researchers to analyse intestinal functions, developmental stages and tumour growth [25, 26]. Transgenic fruit flies (Drosophila melanogaster) are commonly studied to understand the effects of genetic changes. Fruit flies have low maintenance requirements and short life cycle which is reason they are often preferred over other animals. Moreover, they need a comparatively simple genome than several vertebrates, with typically just one copy of every gene. Thus, making phenotypic analysis easy. Drosophila has been researched to study learning, genetics and inheritance, behaviour, embryonic development, and ageing. Transposons (particularly P elements) are well developed in Drosophila providing an early method to add transgenes to their genome. Now, this has been appropriated by more modern gene-editing techniques.

Medicine

Human genetic disorders caused by knocking out genes allow researchers to review the mechanism of the disease and their possible cures. Pigs are an honest choice for research as they have an identical body size and anatomical features, physiology, pathophysiological response and diet [27]. Genetically modified mice are the foremost common mammals utilized in biomedical research, as they're cheap and easy to control. Though, non-human primates are the simplest model organisms almost like humans, but there's less public acceptance towards using them as research animals. Scientists have produced a stable line of transgenic marmosets for amyotrophic lateral sclerosis, Parkinson's disease and Huntington's disease [28]. Human proteins expressed in mammals are more likely to be similar to their natural counterparts in comparison to plants or microorganisms. Stable expression has been achieved in sheep, pigs, rats and other animals. ATryn (antithrombin) is the first human biological drug obtained from GM goat’s milk. It got approval in 2009. This anticoagulant decreases the probability of blood clots during childbirth or surgery [29]. Pigs are genetically modified such that their organs cannot carry retroviruses or have modifications to scale back the prospect of rejection [30]. Genetically modified pig’s lungs are being chosen for transplantation into humans [31]. Moreover, there's scope to make chimeric pigs carrying human organs [32]. GM chicken was created to supply a recombinant form of the enzyme lysosomal acid lipase (LAL) referred to as sebelipase alfa. It helps in treating a rare condition in its egg. It got approval in 2001 and is being sold under the name Kanuma [33]. A genetically modified chicken (Gallus gallus domesticus) has been developed at Roslin Institute which doesn't transmit avian influenza. Genetic modification comprises an RNA molecule that hampers viral reproduction by imitating the genomic region of the flu virus that controls replication.

Conservation

Myxoma virus has been genetically modified to conserve European wild rabbits within the Iberian Peninsula and to help regulate them in Australia. It helped to immunize the rabbits to guard the Iberian species from viral diseases while in Australia, an equivalent virus was genetically modified to lower fertility within the Australian rabbit population [34]. Genetic engineering is often used for the de-extinction of extinct animals. It involves modifying the genome of a close living relative to resemble the extinct one. The attempt has been made with the passenger pigeon [35]. Also, Genes linked with the northern mammoth are added to the genome of an African elephant.

Controlling mosquitoes

By using homing endonucleases after injecting a gene that reduces the development of the malaria parasite, to rapidly spread that gene throughout the male population (gene drive), Malaria-resistant mosquitoes are developed [36]. Using an equivalent approach but with a lethal gene, the populations of Aedes aegypti mosquitoes, the supreme carrier of Zika and dengue virus were reduced by 80% - 90% [37]. Sterile Insect Technique (SIT) is additionally an efficient method. During this technique, there is a competition between genetically engineered sterile males and wild males to mate with the females. Females mating with sterile male produce no progeny, subsequently, reduce the population. Similar approaches have also been followed for controlling Diamondback moths. Pilot projects by Oxitec Company have taken place in the Cayman Islands, Brazil and Panama for controlling the mosquito population [38]. Oxitec is additionally applied in Florida to release genetically engineered mosquitoes. Further, there is plan of releasing self-limiting mosquitoes in Burkina Faso, Africa [39].

Detecting pollution

GM zebrafish is being developed to detect pollution. Fluorescent proteins are attached to genes activated by the presence of pollutants after which the fish glows and used as environmental sensors [40]. GM frogs are used as pollution sensors, particularly for endocrine-disrupting chemicals [41].

Industry

The larvae stage of *Bombyx mori*, i.e. Silkworm is of economical importance in sericulture. Scientists are researching developing procedures to reinforce silk quality and quantity. Silkworms are introduced that produce spider silk which is stronger than normal silk [42]. There's also an opportunity to form other valuable proteins by using the silk-producing machinery. Variety of proteins expressed by silkworms include; human collagen α-chain, human serum albumin, mouse monoclonal antibody and N-glycanase [43].

Pets

GloFish is genetically modified fluorescent zebrafish present in red, bright green and orange fluorescent colours. It was originally developed to detect pollution, however, now it's a part of the ornamental fish industry. In 2003, it became the first genetically modified animal available publically as a purchasable pet [44]. Scientists in Vietnam inserted a mixture of jellyfish proteins and gold dust into the eggs of a seahorse by using the gene shooting method. The green fluorescent bunny glows in the dark. It is created by infusing fluorescent jellyfish protein in a rabbit egg which is later fertilized.

Conclusion

There are a lot number of applications of GMOs by which mankind is highly benefitted such as medical care, food, industry, conservation and research etc. But there is a need to use them wisely to improve economy without doing more harm than good and make the most of their potential worldwide. Nevertheless, the full potential of GMOs will be exhibited with the risks associated with each new GMO on a case-by-case basis.

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Conflict of Interest

The authors have declared no conflict of interests exist.

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