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Genetically Modified Organisms and Biomedical Research

Defining Genetically Modified Organisms or GMOs

Today's domesticated plants and animals are all the result of selective breeding programs. All these organisms have been 'genetically improved' for traits such as yield, or disease and insect resistance, or to produce teacup sized dogs.

A Genetically Modified Organism is an animal, plant, or microorganism that has genes which have been modified using the gene technologies of molecular biology. This is a process where the traits or characteristics of an organism are changed by modifying genes within a species or transferring individual genes from one species to another transgenics). The modification of genes can occur by: eliminating certain genes altogether within an organism, modifying genes by turning them off or on, or altering their location, or adding copies of specific genes from other organisms. Other associated terminology includes genetic engineering, and transgenics or recombinant DNA (inserting a gene from one species to another).

While the human race has methodically modified crop plants and animals through selective breeding for thousands of years, genetic engineering allows that time-consuming process to be accelerated, and to allow for traits from unrelated species to be introduced.

When people talk of genetically engineered or modified products like corn or soybeans, they most likely mean *transgenic* organisms. Transgenic organisms mean that a gene from one species or organism has been inserted into the DNA of another species.

By far the most common genetically modified (GM) organisms are crop plants. It is estimated that 60-70% of packaged grocery products contain some GMO ingredients (such as corn syrup, or canola or soybean oil). The technology however has now been applied to almost all forms of life, from fish that glow under UV light, to bacteria that form HIV-blocking "living condoms", from pigs bearing spinach genes, to goats that produce spider silk.

GMOS in Biomedical Research

The use of genetically modified organisms represents an ***enormous*** advance in the biological sciences and medical research, with GMOs are playing an *increasingly* important role in the discovery and development of new medicines. Most diseases, from cancer to dementia, are partly caused by our genetic makeup and over 10,000 diseases are caused by a single faulty gene. GMOs can help researchers understand the workings of human ***and*** animal genes, and allow researchers and scientists to better understand the role of genes in specific diseases.

GMO-based medical research is also fundamental to developing new ways to create and produce vaccines to prevent disease (for example a vaccine for HIV), to develop new and more efficient ways to create antibodies for the treatment of disease, and to develop and manufacture pharmaceuticals. For example, until the mid-1980's most insulin was produced by extracting a human-equivalent insulin from the pancreas of animals (usually pigs). Thanks to GMO-based research, the genetic sequence for insulin was removed from human DNA, and then inserted into the DNA of a bacteria (Escherrichia coli -E. coli). Insulin for treating diabetes has now been produced with this genetically engineered bacteria for more than 20 years (25.8 million Americans have diabetes and it is the seventh leading cause of death in the United States). Work is developing the production of insulin now in the safflower. Genetic modification in bacteria has also resulted in the production and marketing of human growth hormone inhibiting hormone, Somatostatin, and a genetically engineered version of erythropoietin, a protein that simulates the formation of red blood cells. In 2012, the U.S. Federal Drug Administration approved the first drug for humans that was produced in a genetically engineered plant cell (carrots). The drug, called Elelyso, is a treatment for a disorder known as Gaucher disease that results from the lack of a specific enzyme.

Research on antibodies and vaccines developed through recombinant DNA and genetic modification is also an important research area. For example, a new vaccine being developed is based on genetically modified peanut proteins and could potentially protect people with peanut allergies from developing a life-threatening allergic response and human trials have begun on an antiviral drug synthesized by genetically modified tobacco plants to establish its safety and use to prevent HIV infection.

Because isolating antibodies in large quantities is difficult and expensive, genetic engineering offers great promise for not only developing treatments and cures, but also in making such treatments widely available and affordable by being able to lower the time and cost for vaccine production by production in GMOS plants to the high standards needed for their use in humans.

Often called "biopharming", genetic modification within a plant allows for researchers to more rapidly develop organisms that exhibit certain characteristics, produce needed biologicals, or offer genetic models necessary for medical research and the development of treatment, vaccines, or cures. In addition, the treatment for numerous human (and animal) aliments such as cancer, herpes, and infectious diseases require human and viral proteins (antibodies, enzymes, etc.) that can only be derived from living systems. Currently, the majority of these drugs are based on such material taken and cultivated from animal cell cultures. However, the production of such needed antibodies from animal cells is expensive, making the resulting drugs too expensive for most patients. Second, and more critical, there are simply not enough of these materials being produced to meet existing demand, much less projected future demands based on the number of new drugs in development. Many genetically modified plants have already proven critical information and are in use to produce such necessary antibodies, and continue to offer great promise. Pond algae, tobacco plants, and soy are only a few of the many plants that have contributed greatly to medical advancement. Exploration and continued development of GMO-based protein expression is necessary if we are to produce affordable, life-saving medicines for the future. There are no current means to express such proteins outside of living cells.

GMOs and Transgenic Animals

While most often regarded as a crop or plant issue, "Genetically modified organisms" or GMOs also includes genetically modified animals that are frequently a part of biomedical research. Like other forms of genetic modification, animals can be genetically modified in several ways, for example by removing genes from its DNA structure or by adding new. Gene knockouts allow researchers to delete individual genes from animals, giving us valuable clues as to what those genes do. In others modifications, researchers introduce new genetic material into suitable hosts (typically rodents), from other species, often human. Commonly referred to as transgenic, these animals have been genetically engineered/modified to create new or isolate existing characteristics. In many cases this has no noticeable effect, while in some cases the alteration leads the animal to develop the equivalent of a human disease being studied.

These transgenic animals have proven to be an important way to not only study a disease, but also to treat or even cure a disease. As an example, to get specific human antibodies for use in drug development, mice have been developed that are capable of making fully human antibodies, in place of the normal mouse antibodies that are normally generated. Such mice can be injected with cells or material from a human tumor or an infectious agent. The mice respond with a human antibody response instead of a mouse antibody response. Researchers then immortalize the antibody-producing cells from the mice into special nutrients so they multiply, producing therapeutic quantities of monoclonal antibodies. As a result of such research, at least 33 fully human antibodies have been tested in human clinical trials to date. These antibodies are analogous to approved antibody therapeutics such as Erbitux for colorectal cancer; Remicade and Humira for rheumatoid arthritis; three drugs for preventing organ transplant rejection and Xolair for asthma. While almost all of the aforementioned antibodies are originally mouse in origin, the transgenic mice that produce fully human antibodies are a potential advantage over these therapeutics as their antibodies are fully tolerated in humans; mouse-derived antibodies can be quickly rejected. None of these advances would have been possible without research using genetically modified organisms.

Other examples of GMOs or transgenic animals being used in medical research include transgenic goats to produce TPA or tissue plasminogen activator, and Antithrombin 3 for the treatment of blood clots; Factor 8 and factor 9 being produced in sheep for the treatment of blood clotting disorders such as hemophilia; and human protein C in pigs for use as an anticoagulant; the development of CFTR for the treatment of cystic fibrosis; and the production of MSP-1 antigen in transgenic mice. MSP-1 produces a human antibody response to malaria, and could be the basis for an eventual malaria vaccine. Researchers are developing techniques for gastrointestinal disturbances, rheumatoid arthritis, Alzheimer' s Disease, and cures and vaccines for hepatitis and herpes infections. Researchers are working with dairy cattle to produce milk with an inactive b-lactoglobulin milk protein so that people with lactose-intolerance can eat dairy products. Another role genetically modified or transgenic animals play in research is xenotransplantation – the production of tissues and organs in animals for human use. New heart valves from pigs are an important example.

Pharmaceutical products derived from genetically modified organisms are also developed for veterinary use. An example is the use of a recombinant vaccine-rabies virus for vaccinating foxes against rabies, which is more efficacious and safer than the conventional attenuated SAD B19 strain. This strain, which is still used sometimes, is pathogenic for some non-target mammals. Another is the recombinant Merial canarypox DNA vaccine (for West Nile Disease) that incorporates WNV membrane and envelope proteins into the canarypox DNA and expresses these proteins following administration. Research is also currently underway using forms of GMOs to address Bovine Spongiform Encephalopathy (BSE - mad-cow), various influenzas, feline HIV and leukemia, among many others.

Concerns Regarding GMOs

One of the most common fears about GMOS in the plant world is the possibility of plant-based GMOs mixing with food supplies with resulting health issues, or the potential of transgenic animals breeding with native population. To prevent this, biomedical researchers have turned to producing the pharmaceutical products in non-food, or feed crops such as tobacco (Nicotiana tabacum), duckweed, and others to produce a wide range of human proteins to treat illness, including anticoagulants, growth hormone, Hepatitis C and B treatments, human interferon, liver cirrhosis, human serum, and cystic fibrosis. Regulation of transgenic organisms, including genetically modified or transgenic plants, is shared by three agencies: the Environmental Protection Agency, the Food and Drug Administration, and the USDA – and at the local level, the California Department of Fish and Wildlife oversees transgenic aquatic species. Research facilities are secure, research animals carefully housed and cared for, and no transgenic animal is allowed to breed with wild populations.

In addition, the United Nations, World Health Organization, American Medical Association, the FDA, and the National Academy of Sciences have examined the health and safety issues of GMOs. The UN reported that genetically modified crops "pose no more risk than conventionally grown crops" and "there have been no verifiable reports of their causing any significant health or environmental harm."

There are also concerns about the use of transgenic animals in research. In particular, that these animals suffer more abnormalities, are more likely to be destroyed and that they could have a negative impact on wild populations if they are accidentally released. All animal-based research is subject to rigorous government regulation and inspection.

In addition to profoundly advancing biomedical research and by association offering dramatic developments in medical treatment and improvements in human and animal health, using genetically modified animals can be good for animal welfare because: Fewer animals can be used for each experiment because researchers get more accurate results; the use of transgenic mice is helping to reduce the number of other animals needed for medical research. For example, one pharmaceutical company has helped develop a new safety test for the polio vaccine that uses transgenic mice, rather than monkeys; researchers can use simpler animals like fruit flies and earthworms, or rats and mice instead of using complex animals like primates; and in many cases, researchers don't even need to take blood samples from animals to test for proteins because they can get them to produce those proteins in their milk.

Benefits of Biomedical Research

Nearly every major medical advance of the last 100 years has depended largely on research with animals. We have made significant progress against diseases such as polio, small pox, cancer, heart diseases, and diabetes among many, thanks to animals. Our best hope for developing preventions, treatments, and cures for diseases such as Alzheimer's, AIDS, diabetes, cancer, and treating human and animal conditions will involve biomedical research on a wide spectrum of genetically modified plants, animals, and bacteria. The impact that GMOs have made, whether speaking of GM bacteria or GM cows, is immeasurable, saving lives and improving animal *and* human health *today*.