Gene Editing In Monkeys

It all started when researchers around the world started unraveling different techniques to clone animals and improve human diseases. Establishing perfect animal models is important, especially for the study of human diseases but transgenic technology is believed to be useful for generating animal models. Since the birth of the first transgenic mouse, hundreds of transgenic animal models have been created and have made an excellent contribution to scientific research. There, researchers used Macaca fascicularis, a type of monkey that has learned to live with humans and adapt to some of our states like Florida. Macaques can also be a threat to humans by carrying transmittable and fatal diseases. Researchers said that with a cloned gene edited monkeys, scientists could be able to cure cystic fibrosis and sickle cell anemia for humans. Together, the research raises many ethical and unethical issues because there were many that preceded the births of these five monkeys. To create the edited monkeys, the team started with 325 cloned gene edited embryos and 65 surrogate mothers. This followed in 16 pregnancies but only five monkeys were born. Cloning monkeys are inefficient and expensive now, scientists say that it's better to experiment on mice because research in mice is also more accepted by the public, and the animals are cheaper and quicker to produce. Other researchers have also done studies on these monkeys and have edited the genomes to create models of diseases like severe immune disorders. It is hoped that the accuracy of gene editing combined with stem cell technology could generate ideal disease models, which will be useful in overcoming human diseases.

Background on Species

The long-tailed macaque, or also referred to as the crab-eating macaque is scientifically named Macaca fascicularis and is native to Southeast Asia. The Macaca fascicularis is a cercopithecine primate, cercopithecine is a “subgroup of the Old World Monkeys, which encompasses several species, including macaques, vervet monkeys, mandrills, and baboons.”(NCBI). Old World Monkeys are a “diverse group of primates in terms of body size, habitat, and social organization. They encompass two subfamilies, the colonies, and cercopithecines.”(Lawrence, Cords). With its many names, when in laboratories this species is referred to as the cynomolgus monkey. (Rosso, Badino, Ferrero, Costa, Cordero, Steidler).

The long-tailed- macaque is given its name due to its tail, which is often longer than its body. The tail typically measures about, “16–26 in, which is used for balance when they jump distances up to 16 ft.” (Cawthon Lang). The body length of the adult, which varies among subspecies, is “38–55 cm (15–22 in) along with relatively short arms and legs.” (Cawthon Lang). Males are significantly larger than females, weighing “11–20 lb compared to the females weighing in at about 6.6–13.2 lb.” (Cawthon Lang). The upper parts of the primates body are “dark brown with light golden brown tips, while the under parts of the body is light grey with a dark grey and brown tail.”(Cawthon Lang). Long-tailed, macaques have “backward-directed crown hairs which sometimes form short crests on the midline.”(Cawthon Lang). The skin on their feet and ears is black, whereas the skin on the muzzle is a light grayish pink color. The eyelids often have prominent white markings and sometimes have white spots on their ears. Males have a “distinct mustache and cheek whiskers, while females have only cheek whiskers.”(Cawthon Lang).

Macaques live in social groups that contain, “three to 20 females, their offspring, and one or many males.”(Van Noordwijk, Van Schaik). The groups typically have fewer males than females when considering the male to female ratio. In the social groups of macaques, a clear “dominance hierarchy is seen among females.”(Van Noordwijk, Van Schaik). Females have their highest birth rates around “10 years of age and completely stop bearing young by age 24.”(Van Noordwijk, Van Schaik). Male long-tailed macaques “groom” females to increase the chance of mating.(Gumert). It is said that a female is more likely to “engage in sexual activity with a male that has recently groomed her than with one that has not.”(Gumert). After a gestation period of “162–193 days, the female gives birth to one infant. The infant's, weight at birth is about 11 oz.” (Bonadio). Infants are born with black fur which then turn to a “yellow-green, grey-green, or reddish-brown shade (varying on the subspecies) after about three months.” (Cawthon Lang). Crab-eating, macaques usually do not consume crabs as their main food source; rather “they are considered omnivores, eating different animals, plants, fruits, and seeds.”(Bonadio). Fruits and seeds make up “60 - 90% of their diet, as they also eat leaves, flowers, roots, and bark.”(Bonadio). They occasionally prey on, “vertebrates including bird chicks, nesting female birds, lizards, frogs, fish, invertebrates, and bird eggs.”(Bonadio).

The crab-eating macaque lives in a wide variety of habitats, including “primary forests, disturbed and secondary forests, and riverine and coastal forests of nipa palms and mangrove.”(Bonadio). The native range of this species includes most of “mainland Southeast Asia, from extreme southeastern Bangladesh south through Malaysia, and the Maritime Southeast Asia islands of Sumatra, Java, and Borneo, offshore islands, the islands of the Philippines, and the Nicobar Islands in the Bay of Bengal.”(Bonadio).

This species has a long history alongside humans and even more recently, the subject of medical experiments. In laboratories these monkeys are widely being used in many types of studies, “pharmaceutical, toxicological, pharmacological, metabolic, physiological and psychological research and development.” (Rosso, Badino, Ferrero, Costa, Cordero, Steidler).

Positive in Gene Editing

In the article “Chinese effort to clone gene-edited monkeys kicks off” by David Cyranoski, briefly talks about how monkeys (Macaca Fascicularis) share many genes similar to humans. Using these monkeys as models help scientists study high cognitive functions and brain disorders that are found in humans. “Primates are the best animal model for studying higher cognitive functions and brain disorders in humans” (Chinese effort to clone gene-edited monkeys kicks off).

A group of scientists at the Institute of Neuroscience experimenting some Macaca Fascicularis’ had done gene-editing to weaken a gene in monkeys that are pivotal to their sleep-wake cycle. Scientist used that gene to clone one of the monkeys to evolve five primates with nearly the same amount of information to then begin the experiments for beneficial reasons.

The scientists had found a gene that monkeys have that is connected to brain a disorder in humans. There were many genes that were connected with human diseases. For example, Alzheimer’s disease which is the most familiar kind of dementia. Alzheimer’s disease is one of the diseases found in the orthologous gene list that scientists are looking into to look for some treatments/ a cure. “ By eliminating genes that cause diseases, doctors could treat a wide

range of illnesses, from hearts disease to Alzheimer's" (5 reasons why gene-editing is both terrific and terrifying). Alzheimer's, disease that irreversible and slowly obliterates memory, thinking skills and, the ability to do the simplest tasks. The exact cause of Alzheimer's disease are not completely understood, but at the core are problems with the brain proteins that have failed to properly function, distort the work of brain cells (neurons) and release series of toxic events. Neurons are then being damaged, they lose connections to each other and eventually the neurons from the brain die.

The damage often starts in the are of the brain that controls the memory, but the process start years before the first symptoms that cause Alzheimer's. The loss of neurons spread in a somewhat foreseen pattern to the further areas of the brain. By the later stage of Alzheimer's , the brain had already been smaller in size notably. It is caused by the buildup of a protein called Beta. Researchers have observed under microscopes alongside a sample of this protein, one from a human and the other from the monkey. The scientists have discovered that Macaca Fascicularis also carries this protein but, yet only humans get Alzheimer's and not the monkeys. More fulfilled and sequenced annotations of these genes can be useful to the evolution, and the advancement of human disease models of monkeys.

If a scientist was to keep using monkeys to gene edit and experiment certain types of experiments for related diseases that humans do, there could be a possible cure to be discovered. Gegen editing was also used in monkeys to disable a gene all through the liver that had caused lower blood cholesterol levels that proposed treatment for heart disease. Heart diseases that are caused by abnormal heartbeats. The term 'heart disease' is often used subsumable with 'cardiovascular disease.' Cardiovascular disease mainly calls attention to conditions that include small or clogged blood vessels that can lead into heart attacks, chest pains, or strokes.

There are many benefits from gene- editing Macaca Fascicularis because of the similar genes and functions as humans. B gene levels more exact and study the evolution of gene outlines that connect humans and monkeys more steady.y gene-editing the right gene, correctly, it can be the start of a new cure or treatment like how it has started for Alzheimer's and heart diseases. The recent curated gene annotations have authorize scientists to map

Negative in Gene Editing

Even though many people believe that the successfulness of cloning Macaque Monkeys by somatic cell transfer is a spectacular start to finding the cure to innumerable human diseases including cancer (Cloning of Macaque Monkeys by Somatic Cell Nuclear Transfer), there are people who question whether or not the end results justify the means. The results of genetic editing of the Macaque Monkeys are not only uncertain but extremely high-priced. As stated by the team in Shanghai and the head scientist, the approximate amount spent to create only five genetically identical, cloned Macaques was near $500,000 (Chinese effort to clone gene-edited monkeys kicks off). The process of cloning living beings, in its own, is a whole risk because it isn't a known fact that it will work, for each live birth it is common to have plenty failed attempts in the process between creating, implanting and bringing the clone to terms.

The ethical questions of how an animal should be treated arises, especially in regard to the Macaque Monkeys, because of their cognitive sophistication. A study done on November 2016

by the National Institute of Advanced Studies in Bengaluru, India regarding animal cognition, focused on Macaque Monkeys and how they are able to communicate in order to request grooming from another member in specific areas (Animal Cognition). In the research on finding a valid cure for certain diseases, it is important to find animals that are genetically similar to humans. Because grooming, there, represents proper communication, and the ability to build connections with one another, these primates are the best non-human model for studying brain disorders (Gene-edited Disease Monkeys Cloned in China). The more genetic uniformity between species, the more accurate the research results will be. If the Macaque Monkeys were chosen for this experiment, it was because of the similarities shared with human beings.

The Macaque Monkeys are being cloned to be tested on, to be genetically manipulated and used as research tools. These animals are being inflicted unnecessary suffering by having diseases forced upon them that do not belong in their bodies. Scientists at the Institute of Neuroscience, better known as ION, which is located in Shanghai, China, where the cloning of the first monkeys was achieved, stated that they forcibly disabled a gene crucial to the monkey's sleep cycle called BMAL1 (Chinese effort to clone gene-edited monkeys kicks off). This specific gene is described as an inner clock, which allows a healthy sleep cycle. Not only are researches messing with a vital gene for healthy living but they are editing the genomes of the Macaque Monkeys to inflict them with diseases. The absence or dis-normality of the BMAL1, which has been confirmed as a factor in playing the role of keeping glucose, and the metabolism balanced, is connected with the presence of diabetes, hypertension, depression, and even Huntington's disease (Chinese effort to clone gene-edited monkeys kicks off). All the diseases inflicted on the monkeys are incurable and just like humans, the monkeys undergo the undesirable symptoms. To name a few symptoms; becoming socially withdrawn, extremely irritable energy loss, excessive thirst, and hunger, blurred vision, nausea, difficulty breathing, constant pounding in chest or ears and even harmful behavior. Macaque Monkeys were chosen for this experiment because of the similarities shared with human beings. Cognitive similarities are not the only type of similarities. Human beings, as well as animals, are alive, which makes them entitled and able to feel pain as well as emotional connections. Inflicting pain on an innocent being who understands that they are being harmed is monstrous (The Moral Status of Animals). The conditions that they are being forced under, cause the monkeys to undergo constant discomfort and suffering, making this experimental procedure be considered as unethical.

When regarding life, many find themselves conflicted because it is something that most people hold as valuable. There is always going to be constant conflicts between opposing parties who support different opinions. There are some who are completely against inflicting suffering on innocent beings and others who would go past that and perhaps cross a line, to focus on the positive outcomes that this might bring for the future of the human race.

What it Could Lead into the Future

What this experiment could do for humanity in the future is far beyond what technology has done for us today. Scientist having the ability to clone monkeys with similar to perfect DNA sequencing can be used to further the research of unknown matching disorders in humans and their hope to be cured. This would also reduce the numbers of experiments on other animals. Some people will still argue that it is unethical, though the Macaque monkeys would be cloned specifically for finding cures without the obstruction of causing extinction in the species itself.

This option sounds great at the face of value in determining the new face of medicine but there are things the community have put into consider. The first question that is always asked is; How do we determine which animals are best represented for the research. Due to the similarities in the gene structure in humans and monkeys they are prominently the best choice of other animals that have been recorded in previous experiments. Dolly the sheep was the first animal to be cloned in 1996, creating a basis for other animals to be cloned for further experiments. Scientists have been trying to find an animals that's DNA is similar enough to the DNA sequencing of humans as well as resistant to the technique. Over 23 animals have been tested for cloning and none of them have the proper structure needed to match the humans to begin testing for the diseases. Many people have asked why rats cannot be used for testing since they are the go to animal used in experiments though, their model is not close enough for humans. Meaning if the scientist where to find a cure for alzheimer's disease in the rat it wouldn't be effective for the receiving patient.While the Macaque monkey brains are so similar to humans, their outcomes from the experiences could tell us more information than a mouse or rat ever could.

A similar question was; Why not do the research on humans, that way the outcome is 100% secure. Though this is true scientist cannot permit the experiments on human subjects as it would result in far more destructive than efficiency. This would also imply the need for consent from humans who obtain the diseases with hoping that the experiments were quick and successful, Resulting scientists in doing treatment on animals that essentially have a lower moral standing than it would on humans.

The ideal test subject would be able to withstand the conditions of the environment while maintaining the health aspects a human would be able to take on. Therefore leading the scientist to a better outcome for the diseases. One thing to keep in mind is that cloning and breeding are ethically different. When speaking of the Macaque monkeys they are used for test subjects not as a moral in the environment rather than a being. They are created for the use of research rather than essential quality. There is no way to do biomedical research without the usage of a test subject.

Technology is advancing faster than ever before, though there aren't any computer models specific of effective enough to do the experiment itself im sure some day there will be. As of right now scientist have the ability to do extensive research, experiments, and develop further hypothesis with the test subjects we have now.

The process of the research will be slow and extensive, but the outcome benefits in all aspects of human is more than a reason to consider the research. According to the CDC , “ Alzheimer's disease is the sixth leading cause of death in the U.S. and is the fifth leading cause among people 65 years and older.” (CDC, P.2). Also, according to the NIH, “In 2018, an estimated 1,735,350 new cases of cancer will be diagnosed in the U.S. and 609,640 people will die from the disease”(NIH P.4) This research can essentially help reduce the mortality rate by thousands if there was a cure. The ethics of cloning the Macaque monkeys for research is a much smaller price asked than losing many more people to diseases when there is an outlet for experimentation.

Conclusion

The long-tailed macaque, also named the crab-eating macaque is scientifically known as Macaca fascicularis. A native to Southeast Asia that has learned to live with humans and adapt to some of our states like Florida. These monkeys are closely related to humans, so it all started when a scientist wanted to try gene editing on them. Many people may believe that the successfulness of cloning Macaque Monkeys by somatic cell transfer is a spectacular start to finding the cure to innumerable human diseases, but some might not know what it takes to do the experiment. Cloning monkeys are inefficient and expensive now, scientists say that it is better to experiment on mice because research in mice is more accepted by the public, and cheaper and quicker to produce. The downfalls of this experiment are that it is extremely pricey to clone primates, it cost over $500,000 for simply 5 monkeys. Furthermore, the team in Shanghai started with 325 cloned gene edited embryos, followed in 16 pregnancies but only five monkeys were born. Not only were there many failed attempts but also all the diseases put onto the monkeys are untreatable and just like humans, the monkeys undergo unpleasant symptoms. The monkeys then become socially withdrawn, loose energy, have excessive thirst and hunger, nausea, difficulty breathing, and more. The conditions that they are being forced under, cause the monkeys to go through constant discomfort and distress, making this experiment to be considered as unethical because of animal cruelty. Even if a scientist were to keep using monkeys to gene edit and experiment certain types of experiments for related diseases that humans do, there could be a possible cure to be discovered. Some diseases that could be cured include cancer, cystic fibrosis, and even Alzheimer's disease. There are many benefits from gene- editing Macaque because of the similar genes and functions as humans. By gene-editing correctly, it can be the start of a new cure or treatment like how it has started for Alzheimer's and heart diseases. However, according to the NIH, “In 2018, an estimated 1,735,350 new cases of cancer will be diagnosed in the U.S. and 609,640 people will die from the disease”(NIH P.4) This experiment can assist by decreasing the mortality rate of millions of people if there was a cure to be found. The morality of cloning the monkeys for research is a much smaller than losing many more people to diseases when there is a way out to be able to help.