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## DNA, Selective Breeding And Mammal Cloning

Humans have been breeding dogs for at least an estimated 14,000 years, it is said to believe that the evolution of the domestic dog evolved from the wild grey wolf (*Canis Lupus*.) As humans began domesticating dogs, they had begun to favour specific traits such as dogs with particular physiques and temperaments, hunting skills, intelligence, behavioural traits and even the simple companionship between man and dog. By selecting the most favourable dogs to breed, humans were unconsciously using artificial selection to advance the breed of dog. (*Canis Familiaris*.) Over time humans have since begun manipulating dogs for that purpose, for the purpose to advance the characteristics of interest in the hope that their offspring inherit and display those desirable characteristics, therefore made to meet the need for human demand. Through the use of artificial selection they were able to create a vast variety of dog breeds. Resulting in many organisms/individuals to vastly differ in appearance, inhibiting particular genetics/DNA. Therefore to embed different qualities essential to excel for their purpose. This potentially causes variation to a species or gene pool which is essential for the survival of an organism. Since then biologists have also recently begun genetically manipulating dogs for desirable traits such as increased muscle mass, stronger running ability, also to create dogs with other DNA mutations, including ones that mimic human diseases for biomedical research purposes. Genetically modifying dog breeds and the use of genetic engineering technology however, has had wider biological implications.

Selective breeding, also referred to as artificial selection is a process used by humans to select two organisms with particular genotypic and phenotypic traits in order to produce favourable offspring who will inherit and display those desirable traits or genes, it is these genes that will then be passed on throughout future generations. In this case humans had selected the two favoured breed of dogs one being female and the other male. They had then crossed them together, therefore resulting in a new generation of the favoured offspring, making it a successful reproduction. This will then in turn advance the organisms of the future generation. For instance each of the favoured offspring has resulted from a female egg fertilised by male sperm, this means that only the best or most favourable offspring will reproduce and the gene pool of the next generation will have a higher frequency of the favoured genes. Over time the traits of the favoured offspring will be displayed more frequently throughout future generations as the favoured offspring reproduce continuously, therefore being passed down throughout generations, continuing in a repetitive cycle.

Through the use of selective breeding it can also be used to eliminate undesirable traits from a breed which can come as an advantage in some cases but can also have negative effects. When one specific trait is desired, certain breed of dogs are often used (manipulated) to create the needed offspring. If that gene pool of dogs results in only that offspring produced with only those desired traits then each subsequent generation will lack other qualities because there is a decrease/lack of genetic variation present. When a gene pool of organisms all have identical desired traits due to human demand eventually outside genetics must be introduced into the gene pool to preserve the traits. If that were to occur, however by doing so this could result in the outside genetics to also then dominate the desired traits and reduce the current gene pools appearance/qualities. Therefore result in the removal/deletion of desired traits/genes from the gene pool causing for what is known as genetic drift. The chances of this happening would be

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highly likely for a gene pool of inbred organisms.

Selective breeding has become easier over time as people as well as breeders have found a more effective way to figure out an organism's genotype, this was first carried out using a test cross, By crossing one organism that is expressing the dominant form of a trait with another of the same species that is homozygous recessive for the same trait, it is then possible to determine the offspring's genotype from the traits expressed in those two species. By doing so it is also then possible to determine or have an ideal concept of the genotype of other organisms from the traits expressed in the offspring. Therefore by crossing one organism of the same species that both possess either homozygous dominant or homozygous recessive genes, breeders can now more effectively cross two organisms of the same species and can then almost guarantee a purebred offspring.

However the use of selective breeding and offspring inheriting "favourable" genetics cannot always be 100% guaranteed as selecting from a breed of dog that only has one or a few desirable traits is not always reliable, this is due to the hidden mutations and hidden genes that can occur, although the phenotype that may seem to be suitable, the genotype (and therefore phenotype) of its offspring may not be suitable. If a female breed of dog was to have a recessive gene in its genotype that was not expressed in its phenotype, and her eggs were fertilised with the males sperm, and the male were to also have a recessive gene in its genotype then it would be highly likely that there would be a chance of the offspring being homozygous recessive, however this would also mean that the particular phenotype expressed in the female breed of dog would also not be expressed in the offspring/new generation. This would have a negative effect on the breeder as they wouldn't realise the result, therefore the offspring being homozygous recessive without the breeders knowledge.

Methods like Marker Assisted Selection (MAS), otherwise known as marker aided selection is an effective method that is now used for indirect selection of a genetic determinant of a trait of interest. (MAS) can be useful for traits that also exhibit low heritability, traits that are difficult to measure, or are expressed in late development. The process of Marker Assisted Selection first include mapping the genetic trait of interest or quantitative trait locus (QTL) of interest by developing various techniques and then use this information for marker assisted selection. If both the marker and gene are located far apart then the possibility of selected individuals being recombinants will be highly likely. The markers used should be closely linked to the gene of interest to ensure that only a minor fraction of the selected individuals will be recombinants. Generally not only a single marker but two markers, preferably RFLP markers are used in order to reduce the chances of an error due to homologous recombination.

Other more efficient methods have been carried out, For instance a source known as Artificial Insemination (AI) is also another effective method that is now used for indirect selection. Artificial insemination is the process of male sperm being artificially inserted into the cervix/vagina of a female dog. The insertion of (AI) is applied to avoid the risky trial and error process of selective breeding. This method is used for the purpose of the potential benefits it provides, these benefits include increased safety of the organism and increased production efficiency. Most males usually produce enough sperm in a single ejaculate to be diluted and extended enough to create over one hundred doses producing many semen samples for reproduction. By using artificial insemination humans are able to more effectively determine the genetic trait of interest providing a more guaranteed result. AI is used for preventing or Eliminating the risk of possible diseases such as brucellosis or CTVT, it can also be useful for

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traits that display low heritability or lack the heritability of the desired gene.

Since humans have begun selectively breeding dogs, problems are arising from a genetic standpoint. This is because certain breed of dogs are often being selected for specific traits and those traits only. For example once those specific genes in dogs are selected for and are consistently being bred due to human demand, other genetics in a dog species of the gene pool will eventually over time be non existent/removed from the population as the favoured genes become more dominant over the other genes in the gene pool, thus replacing those undesirable genes. Once that gene is bred out of evolution it is very difficult almost impossible for you to bring that gene back, therefore the gene for that organism that once existed in the previous generation will no longer exist having a major impact on the ecosystem.

Another biological implication of selective breeding is that it reduces genetic diversity. The lack of diversity in a gene pool between each dog and their alleles due to being closely related would increase the chances of organisms to become susceptible to the same diseases/pathogens. An example of this is inbreeding, inbreeding increases homozygosity. This is because inbreeding can result in both harmful and undesirable genes inherited in both parents to become expressed in their offspring having many negative effects. Continued inbreeding would result in an accumulation of recessive genes which can cause inbreeding depression, this is not a state of mind but rather a physical state resulting in low fertility, poor general health such as weakened immune systems and most importantly inbreeding results in negative/undesirable genes increasing the chances of being inevitably prone to disease. This is of major concern when attempting to protect small populations from extinction. The consequence is that little new genetic information is added to the gene pool, thus recessive deleterious alleles become more increased and evident in the population, eventually resulting in the species of the population to be removed from the gene pool.

Other than the use of selective breeding, humans have also discovered another technique that is now used for the manipulation of dog breeds. This process is referred to as Mammal cloning. With the use of genetic cloning technology biologists are now able to more effectively have more control throughout the process therefore having a much more higher success rate allowing them to introduce certain genes into a dog without having to go through the relatively long and unguaranteed process of selective breeding. By using cloning technology it is now much easier for biologists to add/insert certain genes into a species one may not naturally possess. The purpose of this technology is so that scientists can produce genetically identical copies of a gene from one desired organism to another creating the perfect replica so that those specific genes can still be carried on. They had used a method known as (SCNT) referred to as Somatic Cell Nuclear Transfer. Using this technique scientists select the nucleus of a somatic body cell from the desired breed of dog/nuclear donor and then transfer the cytoplasm of an enucleated egg and insert it into an unfertilised egg cell. Once inside the egg the somatic nucleus is reprogrammed by egg cytoplasm factors to become a zygote nucleus in which the embryo develops into a fetus. The eggs are then inserted into the uterus of a female dog who will serve as a surrogate.

A recent study conducted by Chinese scientists used this genome editing technology to modify a breed of dog such as the beagle. This specific breed of dog has been selected/modified for certain beneficial traits to assist with new DNA mutations, human diseases such as cardiovascular disease, Parkinson's and muscular dystrophy. The beagle came about to explore an approach to new disease dog models for biomedical research. The technique used

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for the beagle is a form of transgenesis which is the process of introducing foreign deoxyribonucleic acid (DNA) into a host organisms genome. This is usually done through experimental manipulation of gametes/ early embryos.They had created a beagle with double the amount of muscle mass by deleting a gene called myostatin, it had then displayed obvious muscular phenotype.

The scientists had developed/modified the beagles by using a supposedly more effective and accurate gene editing tool CRISPR-Cas 9. CRISPR -cas9 consists of two key molecules that introduce a Change (mutation) into the DNA. This is the enzyme cas9 which acts as a pair of molecular scissors that then cuts the two strands of DNA of the beagle at a specific location in the genome so that pieces of DNA can then be added, therefore the hereditary is now existing as the favourable transgenic gene therefore giving it the ability to express the gene encoded by that gene, it also can be used to remove/knockout specific genes.CRISPR -cas9 consists of a piece of RNA called guide RNA (gRNA). The Guide RNA is designed to find and attach to a specific sequence in the DNA. It has RNA bases that are complementary to those of the target DNA sequence in the genome, this means that the guide RNA will only attach to the target sequence and no other regions of the genome. The cas9 then follows the guide RNA to the same location in the DNA sequence. And makes a cut through both strands of DNA. The cut is then repaired introducing mutation. However not all 20 bases need to match for the guide RNA to be able to attach. The problem with this is that a sequence with, for example, 19 of the 20 complementary bases may exist somewhere completely different in the genome. This means there is potential for the guide RNA to attach there instead of at the intended target sequence. The Cas9 enzyme will then cut at the wrong site and end up introducing a mutation in the wrong location, while this mutation may not have an effect on the beagle it could affect a crucial gene or another important part of the genome.

A biological implication of the beagles that have undergone the process of mammal cloning is that there will be very little genetic diversity within the population as the dogs have been cloned and reproduced all from one same dog, meaning all their genes will be identical. In the same way that if affects selectively bred dogs for example inbred organisms, it will also affect genetically modified dogs in the process. Due to the dogs all having similar DNA they will all be susceptible to the Same things or changes in the environment such as particular diseases, health issues for the individuals, for example most dogs that are selected for, a vast majority of those dogs suffer major side effects such as breathing problems in the pug, problems with their immune systems etc, they end up suffering just to assist with a humans satisfaction, those that are cloned are often deliberately created with genetic defects.The use of genetic modification in the long run could significantly decrease resistance to disease and result in undesired traits rather than improve it like intended.

Another biological implication of mammal cloning is the harmful mutations involved with genetic modification. Somatic cells play a significant role in cloning, when a harmful mutation tends to alter these somatic cells in the cloned organism due to gene modification it could then cause the breed of dog to have lethal consequences such as cancer or genetic disorders. Because of these mutations, the affected cells could then possibly divide without limitation therefore resulting in cancer also allowing the cancerous genes to become hereditary. Therefore increasing the chances of generations to inherit cancerous genes/genetic defects.

All breed of dogs that we see today are a product of selective breeding.There are advantages and disadvantages involved with both selective breeding and mammal cloning.In selective

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breeding once humans began to manipulate a certain breed of dog, it had then resulted in the dog's genes to become non-existent/removed from the population. Once this happened there was no going back, the original breed of dog no longer existed. Once the original/previous genes are removed from the population due to human manipulation those genes would be completely lost, therefore making it impossible to undo that. In mammal cloning it has the possibility of a species to also become scarce, as all cloned organisms would inherit identical genetics, therefore the organisms become susceptible to the same things such as diseases etc, resulting in the species to also be wiped out. Although there is a smaller risk of the cloned species being entirely wiped out as the original species will still exist, even after some of its DNA has been manipulated. However both manipulations still decrease genetic diversity and put the species being manipulated at risk. With genetic manipulation becoming more complex, the use of both selective breeding and mammal cloning will still have its limitations and implications.

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