Analysis of Gene and Gene disorders, Genetically modified animal in study of human diseases

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Abstract

Genes are the building blocks of heredity. They are passed from parent to child. They hold DNA, the instructions for making proteins. This paper deals with gene expression patterns and the diseases caused by gene both in animals and human. The gene patterns may vary based on their heredity, so it is important to survey it, before analysing diseases in animal and human. The use of genetically modified animal models has allowed researchers to generate more accurate and appropriate models of human diseases. This has facilitated progress and made more likely that research will transfer to human subjects more quickly.

Keywords: Heredity, Gene disorders, Gene therapy, Diseases

1.Introduction

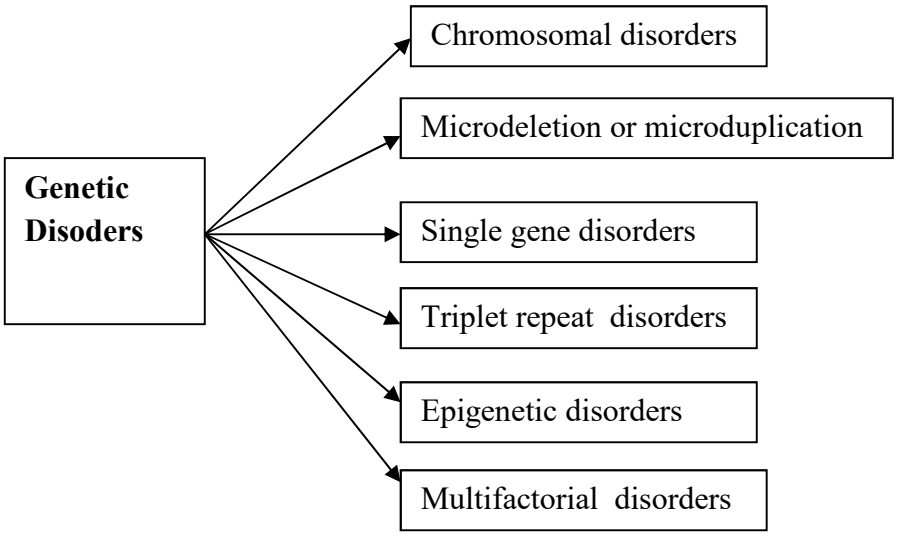
Heredity is the passing of genes from one generation to the next. A person can have changes in a gene that can cause many issues for them. Sometimes changes cause little differences, like hair color. Other changes in genes can cause health problems. The traits an organism inherits is determined during the life process of reproduction. More variation are found in sexual reproduction than by asexual reproduction. In sexual reproduction, the offspring resembles its parents but is also different from them. First, when investigating and understanding the mechanistic basis of disease, as with all comparative analyses, the differences may be as instructive as the similarities. This is a feature that pervades not only comparative genetics but also comparative anatomy, physiology and pathology. Secondly, all or some of the relevant features of the phenotype arising from any mutation may not be detected by the methods commonly used. Some mutations do not result in any observable consequence. This may be due to: (i) the difficulty of detecting very subtle phenotypes (ii) the effects of genetic background that may modify the phenotypic outcome and (iii) the redundancy of pathways involved in biological systems. Thirdly, the disease phenotype resulting from a mutation may be modulated by the person's genetic makeup.

2.Gene and disorders

Researchers have identified more than 4,000 diseases that are caused by mutations. But having a genetic mutation that may cause a disease or condition doesn't always mean that a person will actually develop that disease or condition. On average, people probably carry from 5 to 10 genes with mutations in each of their cells. Problems happen when the particular gene is dominant or when a mutation is present in both copies of a recessive gene pair. Problems can

also happen when several variant genes interact with each other or with the environment to increase susceptibility to diseases.

2.1.Genetic disorders catagories



2.2.Disorders and their Effects

Disorders	Effects	Example	Testing
Chromosomal disorders	Whole or part of a chromosome is missing or duplicated. These are large enough to be seen on a standard karyotype	Trisomy 21, Cri-du-chat, Turner, Kleinfelter	karyotype
Microdeletion or microduplication	Part of a chromosome is missing or duplicated. These are often too small to be seen on a standard karyotype	DiGeorge syndrome, Prader-Willi syndrome (deletion type), Smith-Magenis syndrome, Williams syndrome	FISH – fluorescent in situ hybridization, aCHG – array comparative hybridization
Single gene disorders	A mutation on a single gene. May be autosomomal dominant, autosomal recessive, X-linked.	Cystic fibrosis, Duchenne muscular dystrophy, Marfan syndrome, Sickle cell anemia	DNA sequencing, mutation analysis, deletion testing
Triplet repeat disorders	Exceeding the number of normal trinucleotide repeats in genes. The	Fragile X, Huntington's disease	DNA testing for number of repeats

	normal number varies depending on the gene.		
Epigenetic disorders	The genetic sequence is not changed, but the expression of the DNA is altered	Angleman, Beckwith -Wiedemann syndrome, Prader-Willi (methylation or isodisomy type)	Methylation testing
Multifactorial disorders	Combination of genetics and environment	isolated congenital heart defects, cleft lip and palate, pyloric stenosis	may be available if part of a syndrome, but usually no testing is available

3.Gene therapy

Gene therapy is a one of the promising new field of medical research. In gene therapy, researchers try to supply copies of healthy genes to cells with variant or missing genes so that the good genes will take over. Viruses are often used to carry the healthy genes into the targeted cells because many viruses can insert their own DNA into targeted cells.

4.Genetic disease in human compared with animal

Gene dysfunction is at the root of all genetically determined disease processes. Not all gene dysfunctions are heritable, The gene expression can also be influenced by injury, infection, ageing, cancer, neural degeneration and neural regeneration

4.1.Diabetes

Mutations in the glucokinase gene in humans is the cause of type II diabetes[1] that manifests itself in the young, called maturity-onset diabetes of the young (MODY). Mutations in the glucokinase gene in the mouse also causes type II diabetes, very similar to that seen in human MODY patients.These mutants provide a useful model of MODY and enable scientists to investigate and find the relationship between mutations in the glucokinase gene and the pathogenesis and severity of the disease. Some of the mouse strains carrying mutations in the glucokinase gene that have normal viability and fecundity and that do not appear as detrimental effects on welfare.

4.2.Deafness

The shaker1 mouse mutant[2] displays a profound hearing loss. Researchers identified the mouse gene underlying the shaker1 mutant and then located the corresponding gene in the human genome. It was found that the shaker1 locus was encoded in mice by a gene of the type called myosin. It was subsequently demonstrated that mutations in the myosin gene in humans lead to hearing loss. Some of the mutations in this gene in humans can also lead to a syndrome where there is both hearing loss and blindness at around seven or eight years of age, due to the condition retinitis pigmentosa.

4.3.Psychiatric disorders

It is probable that the equivalent conditions of many human psychiatric disorders[3] are not exhibited in animals because of differences in the brain structures between the two species. It is also the case that many of the human patients who suffer from these disorders do not inherit them through simple genetic determinants, and that environmental factors play an important role. Understanding how these genes function is important for the development of new therapies, although the modification of relevant genes in mice may not necessarily create the neuropsychiatric effects that are exhibited in humans.

4.4.Neurodegenerative disorders

Few neurodegenerative disorders, such as Parkinson's disease and Alzheimer's disease,[11][12] are linked to single gene mutations. In Parkinson's disease, three important mutations in genes responsible for different cellular functions (alpha-synuclein, parkin and a ubiquitin hydrolase) have already been identified. Three different genes with mutations implicated in Alzheimer's disease (beta-amyloid, presenilin and tau) also identified. Reproducing the human form of these mutated genes in animals produces comparable pathologies to those in humans.

4.5.Lesch–Nyhan disease

Mutations in the Hprt gene, which encodes an enzyme involved in metabolism (hypoxanthine-guanine phosphoribosyltransferase), lead to a rare but very severe neurological syndrome in humans known as Lesch–Nyhan disease, the most characteristic feature of which is self-destructive biting. However, Hprt mouse mutants show none of the phenotype characteristics of Lesch–Nyhan syndrome. Researchers found that in the mouse an alternative enzyme pathway ameliorated the effect of the Hprt mutation, and obvious adverse effects on animal welfare from the generation and study of the mutant model have not been detected.

4.6.Cancer

Prior to the sequencing of the mouse genome, investigating spontaneous mutations in genes involved in cancer required approximately 1,000 mice for cross-breeding in order to map a gene to a specific chromosomal region. This region would usually contain several genes, all of which needed to be sequenced to determine which one contained the mutation. Moreover, comparisons between the mouse and human genomes help researchers to find related human genes encoding proteins that could be candidates for the development of new medicines[4][14].

5.Summary of disease caused animal model based on gene expression changes

Disease area	Animal models	Outcome and limitations
Diabetes	Mutants available including type I and type II diabetes models	Insights into genetic pathways involved in diabetes and the hormonal and metabolic control of blood sugar.
Obesity	Mutants available that contribute to obesity under a variety of conditions.	Fundamental insights into the hormonal (leptin) and hypothalamic pathways of obesity have been obtained through the use of mouse models and newly engineered mutants.

Neurological	Mutants available that affect neuronal growth, differentiation and plasticity.	Significant new information on genes involved with the development of neuronal processes. This knowledge is important for the development of therapeutic approaches to neurological disease.
Neurobehavioural	Mutants available that affect a number of endophenotypes of more complex behavioural processes, including: circadian rhythms, learningand memory, anxiety, feeding, sexual behaviour, aggression and maternal care.	None of the available mutants are true models of the complex behavioural outcomes of psychiatric disease in the human population
Sensory	Mutants available that affect both hearing and vision	Significant insights into the genetics of deafness in the human population. While there are many useful models of retinopathies in the mouse, the short lifespan of this species may restrict its usefulness for studying some aspects of retinal degeneration.
Cardiovascular	Several mutant models available.	Some progress, for example, in the study of atherosclerosis through the use of mutants. However, progress in models has been slow and has only just begun to accelerate. Until recently, the rat was a preferred model for studying hypertension and other cardiovascular phenomena.
Cancer	Mutants and strains of mice which show significant variation in both frequency and types of cancer	Historically, a focus of mouse research. While the formation of tumours in the mouse does not always mirror that in humans, many insights into the role of genes that are responsible for causing cancer in mammals have been gained.
Musculoskeletal	Many myopathy models but fewer mutants available that model human bone disease.	Mouse models have provided insights into the genes involved with myopathies in the human population. These mutants have been crucial to developing a better understanding of myopathic processes in humans and in the assessment of potential therapies.
Ageing disorders	Mutants available for Alzheimer's and Parkinson's disease	Considerable progress has been made in understanding Alzheimer's disease, Parkinson's disease and other neurodegenerative disorders.Receptors that could act as targets for future new drugs have been identified.

6.Conculsion

The study of human disease involves, the vast majority of animals that are genetically modified, for this frequently used animals are mice, rats and zebrafish. Although an animal model cannot be considered as an exact replica of a human disease, scientists working in the field have found that there are often sufficient similarities to make informative comparisons. Even when animals do not present disease symptoms that are similar to those of humans, useful information may still be discovered regarding gene function.

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