GENETICS AND GENOMICS

LAB REPORT

Name

Date

Course Name

Exercise 1: Punnett Squares

Introduction

Punnett squares are a widely used method of predicting the chance of occurrence of genetic disorders in offsprings for parents who either carry the disease or are affected by the disease. Parents who have a family history of the disease or manifest symptoms of a disease can benefit from undergoing this test to determine if their children will be a carrier or symptomatic of the disease.

The allele with a disease-causing mutation is denoted with a capital letter (for example, A) and the normal allele is denoted by a small letter (for example, a). There are several types of inheritance that can be identified by making Punnett squares. They are autosomal dominant, autosomal recessive, X-linked dominant, and X-linked recessive inheritance. In case of autosomal dominant disorders, there is a 50% chance that either parent will transmit the disease-causing mutation to their children. On the other hand, in case of autosomal recessive disorders, there is only a 25% chance that the mutation will be transmitted by either parent to the offspring. For X-linked disorders, the pattern of inheritance is different as it depends on which copy of the chromosome is active in the female and whether the child is a boy or a girl.

In this exercise, 4 genetic disorders were considered and they were cystic fibrosis, Tay-sachs disease, a combination of Huntington's disease and cystic fibrosis, and colour blindness. Punnett squares were prepared for each disorder based on the given phenotypic manifestations of the parents and the probabilities of transmitting the disorder to the children were calculated.

Results

Based on the given phenotypes of the parents for 4 specific genetic disorders, the genotypes of the parents were determined and Punnett squares were prepared. The probabilities of the children being affected by the disease were also calculated in each case. The results for each genetic disorder are given below.

1) **Cystic Fibrosis**

Mother's genotype: Ff

Father's genotype: Ff

Cystic Fibrosis		Father	
		F	f
Mother	F	FF	Ff
	f	Ff	ff

Based on the Punnett square, the probability that the parents will have a child with cystic fibrosis is 25% and the probability that their child will be a carrier is 50%. The parents have a 25% chance that their child will neither have the disease nor be a carrier of cystic fibrosis.

2) Tay-sachs disease

Mother's genotype: TT

Father's genotype: Tt

Tay-Sachs Disease		Father	
		T	t
Mother	T	TT	Tt
	T	TT	Tt

Based on the Punnett square, the couple will not have any child who is affected by Tay-sachs disease. However, they have a 50% chance that their child will be a carrier and a 50% chance that they will not harbour the disease-causing mutation in the gene.

3) Huntington's disease and cystic fibrosis

Mother's genotype: hh ff

Father's genotype: Hh Ff

Huntington's Disease and Cystic Fibrosis		Father			
		HF	Hf	hF	hf
Mother	hf	HhFf	Hhff	hhFf	hhff
	hf	HhFf	Hhff	hhFf	hhff
	hf	HhFf	Hhff	hhFf	hhff
	hf	HhFf	Hhff	hhFf	hhff

In this case, Huntington's disease is an autosomal dominant disorder and cystic fibrosis is an autosomal recessive disorder. Based on the Punnett square, there is a 50% chance that the child will have Huntington's disease and a 50% chance that the child will have cystic fibrosis. There is a 25% chance that the child will have Huntington's disease but not cystic fibrosis, and a 25% chance that the child will have cystic fibrosis but not Huntington's disease. There is a 25% chance that the child will not be affected by either disease, and a 25% chance that the child will have both Huntington's disease and cystic fibrosis.

4) **Colour Blindness**

Mother's genotype: $X^{-}X^{-}$

Father's genotype: $X^{C}Y^{-}$

5)
6)
7)
8)
9)

Color Blindness		Father	
		X^{C}	Y^{-}
Mother	X^{-}	$X^{C}X^{-}$	$X^{-}Y^{-}$
	X^{-}	$X^{C}X^{-}$	$X^{-}Y^{-}$

Based on the Punnett square, the couple will not have any child who is affected by colour blindness. All daughters will be carriers of the disease while the sons will neither have the disease, nor be carriers of the disease.

Discussion

Different genetic disorders show different types of inheritance patterns and knowledge of these can help us determine the probability of transmission of disease-causing genes in offsprings. In this exercise, we studied different genetic disorders and saw their inheritance patterns in offsprings. Cystic fibrosis and Tay-sachs disease were autosomal recessive disorders, Huntington's disease was autosomal dominant, and colour blindness was an X-linked recessive disorder. Based on the results, the autosomal recessive disorder has a 25% chance of getting transmitted in offspring whereas autosomal dominant disorders have a 100% chance of getting transmitted to offspring.

Conclusion

Genetic disorders may be either autosomal which means that they are passed down through the autosomal chromosomes, and sex-linked which means that they are passed down through either the X or Y chromosome. In both cases, the disorder may be either dominant where only one allele is required to cause the disease and recessive where two copies of the same mutation are necessary to cause the disease.

In case of cystic fibrosis, both parents were carriers as it is an autosomal recessive disorder. There was only a 25% chance that the child would acquire both the disease causing alleles from the two parents and manifest the symptoms of the disease. There was a 75% chance that the child of the couple would not have the cystic fibrosis phenotype. Tay-sachs disease is also an autosomal recessive disorder, but in this case, only one of the parents was a carrier and the other parent was normal. The child would always inherit the normal allele from one of the parents and thus, not express the phenotype of the disorder.

Huntington's disease is an autosomal dominant disease which means that every child that inherits the disease-causing allele will express the phenotype. Hence, the child of a parent having Huntington's disease has a 50% chance of inheriting the causative allele and expressing the phenotype. Colour blindness is an X-linked recessive trait meaning only men who have a single copy of the X chromosome are affected by it and women having two copies of the X chromosome do not express the phenotype. As men transmit the Y chromosome to their sons, male children of affected fathers do not inherit the disease. On the other hand, men transmit the X chromosome to their daughters and so, all daughters of affected fathers are carriers of the disease.

Exercise 2: Pedigree Charts

Introduction

Pedigree charts are diagrams that represent the inheritance and appearance of phenotypes of a particular gene spanning three to four generations in humans. It is presented as an easily readable chart that helps geneticists track the inheritance pattern of a particular disease in a family and discern if it shows autosomal dominant, autosomal recessive, sex-linked dominant, or sex-linked recessive inheritance patterns.

Pedigree charts use a standard set of symbols where circles represent females and squares represent males. If the gender of a particular person is unknown, a diamond may be used. Persons expressing a particular phenotype are shaded and persons not expressing the phenotype are left unshaded. Carriers, if known, are indicated by a dot in the centre of the symbol.

Relationships between the people are shown by means of lines. Married people are connected by horizontal lines and their offsprings are indicated by vertical lines. More than one offspring are listed in their order of birth. People who have died are represented by a diagonal line across the symbol. Each generation is represented by roman numerals starting from the first generation that can be identified and individuals within each generation are identified by numbers 1, 2, 3 etc. More complicated relationships and events such as twins or triplets, and abortion or miscarriage are indicated by special symbols.

Studying pedigree charts based on the principles of Mendelian inheritance can help us analyze if a given trait is dominant or recessive within a family and understand its inheritance pattern. They are often constructed once an individual with a genetic disorder has been identified to understand the probability of disease transmission to future offspring.

Results

In this exercise, three given pedigree charts were analyzed to find out which of them showed the sex-linked recessive inheritance pattern of hemophilia.

Pedigree chart number 3 given below shows the sex-linked recessive pattern of inheritance.

Chart 3

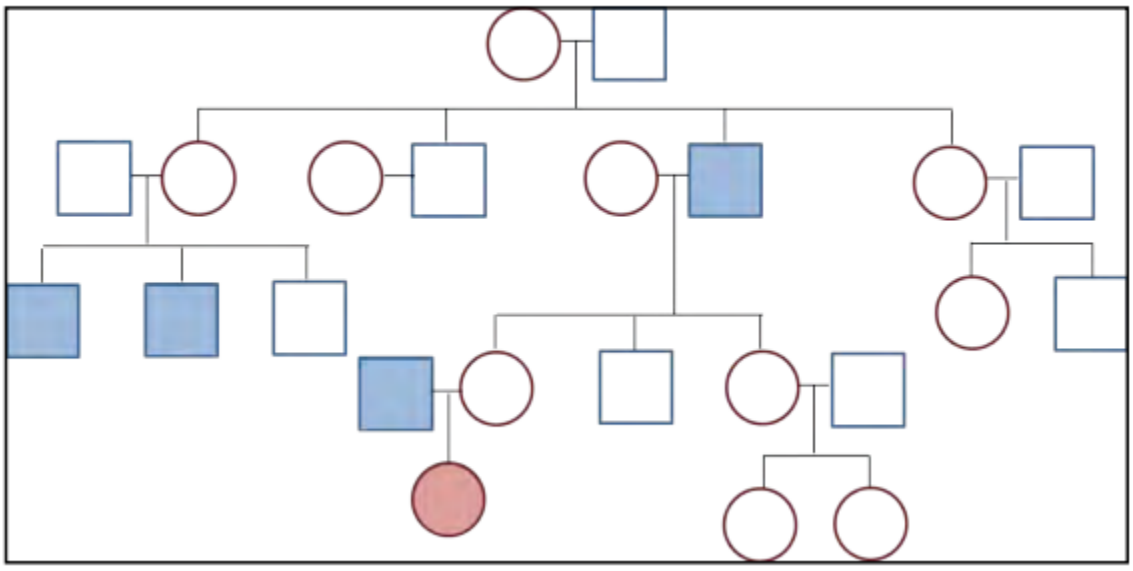


Figure 1: Pedigree chart showing sex-linked recessive pattern of inheritance

Discussion

From the chart, only one male child in generation II expressed the phenotype of hemophilia. As hemophilia is an X-linked trait, the affected male must have inherited the trait from his mother through the X chromosome. Thus, the mother of the affected male must have been a carrier and the percentage of transmission of the disease-causing gene to her offspring is 25% and to male children is 50%. However, as the mother is a carrier of the disease, both her daughters in generation II must also be carriers of the allele.

In generation III, the eldest child has transmitted the allele for hemophilia to 2 of her 3 male children making them express the phenotype of the disease. On the other hand, her other three children have not transmitted the disease to their offspring.

In generation III, the affected male's daughter has married a person with the disease-causing allele and has given birth to a daughter expressing the phenotype. Although X-linked traits only affect males as they have a single copy of the X chromosome, in this case, the mother is a carrier and the father is expressing the phenotype, and so, both have transmitted their disease-causing alleles to their offspring.

Conclusion

Hemophilia is a sex-linked recessive disorder meaning that the disease-causing allele is carried on the X chromosome and two copies of the allele or one copy in case of males is required to cause the disease. It is a disorder in which one of the important factors required in blood clotting process is defective. Males who are affected by this disease cannot transmit it to their sons as they transmit the Y chromosome and not the defective X chromosome to their sons. On the other hand, they transmit the defective X chromosome to their daughters making them carriers of the disease. These carrier females have a 50% chance of passing the defective X chromosome to their sons making them express the phenotype.

In this case, it is evident that the carrier female in the first generation passed it on to one of her sons among her 4 children making him express the phenotype. One of her daughters, who was a carrier, in turn passed it on to two of her three sons making them express the phenotype. When a carrier daughter married an affected male, both of them transmitted the disease-causing allele to their daughter making her express the phenotype.

Exercise 3: Karyotyping

Introduction

Karyotyping is an important part of genetic screening which involves visualizing the chromosomes of an individual to determine his/her chromosome complement. It is a test that is used to view the complete set of chromosomes of an individual to measure the number of chromosomes and see if there are any changes in the number. A karyotype refers to the complete count of chromosomes in an organism and their appearance under a microscope. The features that are noted during karyotyping are length, number, banding patterns, and position of centromeres.

The normal human karyotype consists of 22 pairs or 44 autosomal chromosomes numbered 1 to 22. It also has one pair of sex chromosomes which may be XX in case of females and XY in case of males. Any variation from this standard karyotype may result in severe genetic and developmental abnormalities.

There are several things that need to be noted while viewing a karyotype. The total length of the chromosomes may vary based on the amount of DNA duplication that has taken place during mitosis. The position of the centromere may vary due to differences in translocation. There may be differences in the number of chromosomes due to nondisjunction during crossing over. One or more of these errors may result in phenotypic manifestations that may lead to severe behavioural changes and developmental abnormalities sometimes resulting in death.

Results

In three of the cases, the chromosomal disorder, genotype, and phenotype based on the karyotype were deduced. The results are given in Table 1 below.

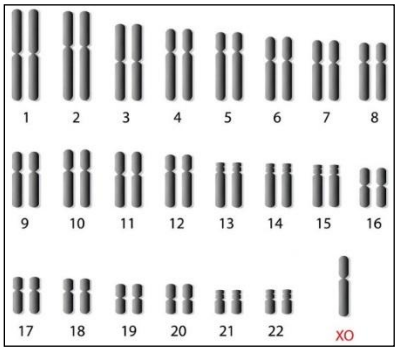
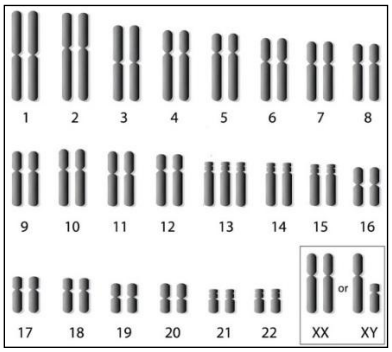
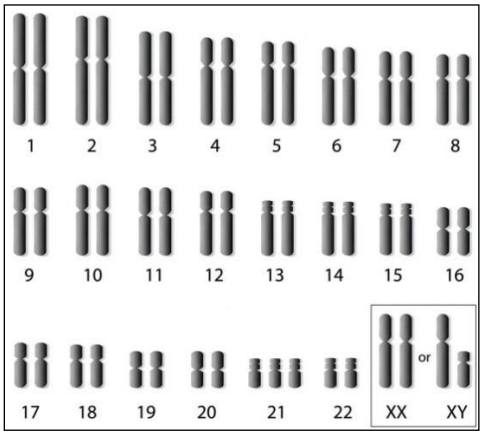
Karyotype	Genotype	Chromosomal Disorder	Phenotype
Disorder 1  © Alila Medical Images	Turner's Syndrome	Only one X chromosome	Only viable monosomy not resulting in death. Reduced height, sterile, normal intelligence
Disorder 2  © Alila Medical Images	Patau Syndrome	An extra copy of chromosome 13	Cleft palate as well as eye, brain, and circulatory defects
Disorder 3  © Alila Medical Images	Down Syndrome	An extra copy of chromosome 21	Delayed cognitive ability, oblique eye shape, flat nasal bridge

Table 1: Analysis of karyotypes for identification of possible chromosomal disorders

Discussion

Given 3 different karyotypes, the chromosomal disorder was analyzed based on the numbers of the autosomal and sex chromosomes. The genotypes and possible phenotypes of each observed chromosomal disorder were also noted.

The presence of three copies of chromosome 21 instead of two indicates Down syndrome which leads to delayed cognitive abilities and changes in physical appearance. Individuals with Turner's syndrome have only one copy of the X chromosome and they are sterile with normal intelligence. The presence of three copies of chromosome 13 manifests as Patau syndrome resulting in significant brain and circulatory defects.

Conclusion

A karyotype is an important tool that is widely used in genetic screening to visualize chromosomal aberrations and predict possible phenotypes in the offspring. During DNA replication and crossing over during meiosis, several errors may happen in the distribution of chromosomes between daughter cells. These errors may result in different types of syndromes manifesting as significant physical, behavioural, cognitive, and developmental changes in an individual. Early detection of these types of genetic disorders can help implement precautionary measures to delay the onset of symptoms in the offspring.

Although a karyotype is very helpful in identifying genetic disorders, it can only help visualize chromosomal aberrations and it cannot give any insight on the genetic level. Even if a person has a normal karyotype, s/he may still carry deadly mutations in the genes that may cause phenotypic manifestations in the offspring. Some examples of this are cancer and diabetes which are not discernable by karyotyping alone and more intensive genetic screening needs to be done to identify these genetic disorders.

The most common types of chromosomal disorders occur due to numerical changes resulting in extra or missing chromosomes in an individual. This may be due to large-scale deletions or duplications of a chromosome resulting in disorders such as Turner's syndrome, Down syndrome, Klinefelter syndrome, Patau syndrome, and Edwards's syndrome. All these disorders are discernible through karyotyping and the possible phenotypes for an offspring can be predicted in the early developmental stages.

Exercise 4: The Human Genome Project

About the Human Genome Project (HGP)

The human genome project was undertaken by a team of international researchers to sequence and map all the genes in the human genome. It began on 1st October, 1990, and ended in April, 2003, and the end result was a complete blueprint of the entire genome of a human. The scientists were able to determine the order of the genes by means of finding out the nucleotide sequence of the gene, prepare maps to indicate the locations of the genes on the chromosomes, and prepare extensive linkage maps which are helpful in tracking the inheritance patterns of genetic traits.

This project has revealed that humans have around 20,500 genes distributed among about three million nucleotides. This information was shocking as previous estimates of the number of genes in humans ranged from 50,000 to 140,000 genes. Around 2,800 scientists were a part of the International Human Genome Sequencing Consortium and they belonged to six different countries which are France, Germany, Japan, China, the UK, and the USA.

The Human Genome Project has far-reaching implications for the field of medicine. Based on the genetics of a particular individual, some people can tolerate certain medicines and others cannot. Sequencing the human genome helps doctors understand the differences in metabolism of different drugs by different individuals. It has provided the basis of medical diagnostic testing for various disorders by techniques such as Polymerase Chain Reaction (PCR). It can help doctors understand the susceptibility of certain individuals for certain diseases and take early precautionary measures. It can also help doctors suggest the right kind of diet for an individual's digestive system.