

Karyotyping with Ideograms

Student Activity

Introduction

When a cell undergoes mitosis its nuclear DNA is tightly coiled into structures called chromosomes. Geneticists can inspect the chromosomes for genetic abnormalities by staining the chromosomes and viewing them using an oil immersion lens on a compound microscope. This technique, called *karyotyping*, allows geneticists to see abnormalities such as extra chromosomes, missing chromosomes, and malformed chromosomes.

Concepts

- Centromeres
- DNA banding
- Chromosomal abnormalities
- Karyotyping

Background

Normal human somatic (body) cells have 46 chromosomes. The 46 chromosomes include two possible types of sex chromosomes, X and Y, and 22 pairs of autosomes. One copy of each autosome and an X chromosome are inherited from the mother. The father provides a second copy of each autosome plus either an X or Y sex chromosome.

If the resulting embryo has two X chromosomes it is a female, while an embryo with both an X and Y sex chromosome will become a male. The autosomes pair up in so-called homologous or matching chromosomes. After staining, each pair of homologous chromosomes is easily distinguished from other chromosomes by differences in length, in the position of the centromere, and by the pattern of bands created using special stains. The centromere is always located in one of three possible positions in human chromosomes (see Figure 1). If the centromere is in the center of the chromosome it is called *metacentric*. If the centromere is located near one end of the chromosome it is called *acrocentric*. The third centromere position may be between the center and the end of the chromosome—this position is called *submetacentric*.

In order to facilitate comparison of the genetic makeup of people from all over the world, geneticists established a classification and naming system, called the *Denver System*, to describe and identify chromosomes. The Denver System was established in 1961 at an international meeting of geneticists in Denver, Colorado. According to the Denver System, the sex chromosomes are named X and Y, while the autosomes are numbered in descending order, with the largest called chromosome 1, and the smallest chromosome 22. The Denver System further subdivides or classifies the chromosomes into eight groups A–G (see Table 2). A *karyotype* is the specific arrangement of specially stained chromosomes using the Denver System.

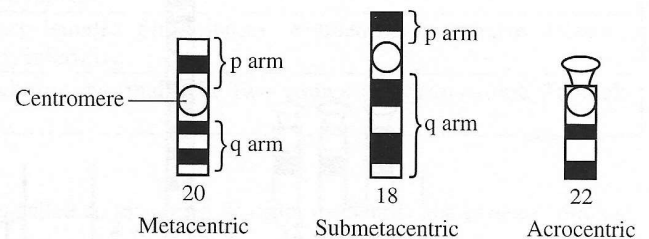


Figure 1. Position of the centromere in human chromosomes.

Table 1.

| Group | Chromosome Numbers | Description |
|-------|--------------------|--|
| A | 1–3 | Long, metacentric |
| B | 4–5 | Long, submetacentric |
| C | 6–12 | Medium, submetacentric |
| D | 13–15 | Medium, acrocentric |
| E | 16–18 | Short, submetacentric |
| F | 19–20 | Short, metacentric |
| G | 21–22 | Very short, acrocentric |
| Sex | X and Y | X—Medium, submetacentric (size similar to chromosome 6) Y—Very short, acrocentric |

Problems occurring during mitosis and meiosis can result in cells containing too many or too few chromosomes or parts of chromosomes. Other problems may occur if part of one chromosome breaks off and becomes attached to a different chromosome. The consequences of chromosomal abnormalities can vary from fatal or to insignificant, depending upon the size and location of the error and when the error occurred. For example, an embryo with three copies of chromosome 1 will result in a miscarriage, whereas cancer may occur when specific genes are deleted from chromosomes during mitosis in an adult.

There are two basic types of genetic abnormalities that can be detected by geneticists using a karyotype—numerical errors and structural errors (see Figure 3). *Numerical errors* include trisomy, in which three copies of a chromosome are present instead of the usual two, and monosomy, in which only one copy of a chromosome is present. *Structural errors* occur when part of a chromosome is missing or not located in its correct position. There are four types of structural errors—translocations, inversions, deletions, and duplications. *Translocations* arise when part of one chromosome breaks off and attaches to another chromosome. Chromosomes with acrocentric centromeres (centromere near one end) such as chromosomes 13, 14, 15, 21, and 22 have very short p arms that break off rather easily. The remaining long q arm may translocate and stick to another acrocentric chromosome (see Figure 2). *Inversions* involve a section of chromosome breaking off and then reattaching to the same chromosome upside down. If a section of a chromosome is completely absent it is called a *deletion*. *Duplications* occur when a section of the chromosome is repeated.

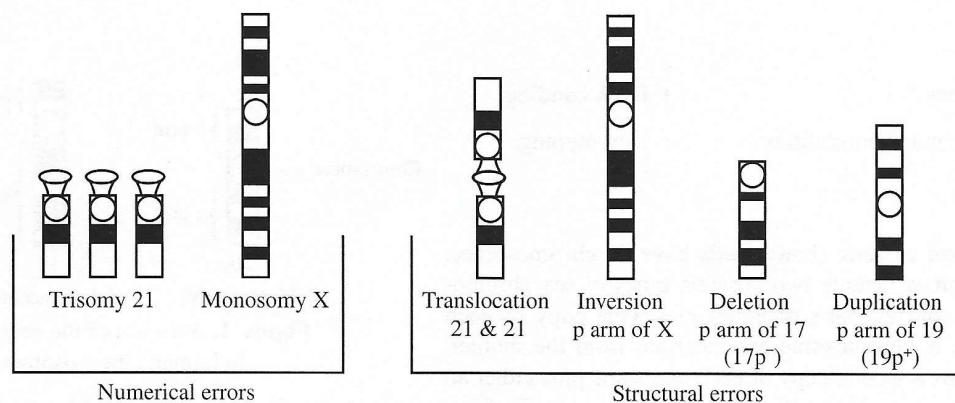


Figure 2.

In some cases the chromosomal abnormality is present in the gamete (egg or sperm cell) due to problems in meiosis. A faulty gamete will produce an embryo in which every cell contains the abnormality. Full numerical abnormalities are usually fatal and the embryo miscarries. The few exceptions are Monosomy X (one X), Disomy Y (two Y's), and Trisomy 13, 18, 21 or X (three copies of the same chromosome). Surviving full structural abnormalities are not always severe because the extent of the change from "normal" varies.

Mosaicism occurs if the chromosomal abnormality occurs during mitosis in the embryo. A *mosaic* is one organism with two different genotypes—some of the cells will have a normal set of chromosomes, while others will have the abnormal set of chromosomes. The severity of abnormality in a mosaic can be mild or severe depending upon how old the embryo is when the error occurs and how much of the chromosome is in error. If the error occurs late in development, very few cells will carry the error and the organism will have mostly normal-functioning cells with either mild problems or even no problems. If the error occurs early in development then a majority of cells will carry the error, potentially resulting in severe problems such as mental retardation and heart defects.

The karyotypes of a normal male and female, as well as individuals with different numerical errors are provided in this activity. Table 2 summarizes the genetic composition of each individual whose karyotype is included in this activity. The genetic composition of the karyotype is summarized as follows: first, by the number of chromosomes present in the cell (45, 46, or 47); then by the sex chromosomes present (XX, XY); and finally by the number of any abnormal chromosome (21, X, etc.). For example, 47,XXY is a male with two X chromosomes and one Y chromosome instead of the usual one X and one Y.

Table 2.

| Name of Syndrome | Genetic Composition | Frequency and Characteristics of Affected Individuals |
|-------------------------|----------------------|---|
| Down Trisomy 21 | 47,XX,21 47,XY,21 | 1 in every 800–1000 newborns. Short stature, characteristic facial features, heart defects, poor muscle tone in infancy, mild to moderate mental retardation. |
| Edwards Trisomy 18 | 47,XX,18 47,XY,18 | 1 in every 3000–5000 newborns. 95% die before birth, of those that survive <10% survive to their first birthday. Short stature, abnormally shaped head, heart defects, defects in most organ systems, seizures, moderate to severe mental retardation and motor delays. |
| Patau Trisomy 13 | 47,XX,13 47,XY,13 | 1 in every 5000–10,000 newborns. More than 80% die before they are one month old. Less than 5% live past their first birthday. Extra fingers and toes, deformed feet, small head, cleft lip and palate, small or absent eyes, malformed brain, heart and kidney defects, severe mental retardation. |
| Klinefelter | 47,XXY | 1 in every 500–1000 newborn males. Low levels of testosterone lead to the development of some breast tissue and infertility; learning disabilities are common. |
| Disomy Y YY | 47,YYY | 1 in every 1000 newborn males. Tall stature, delayed speech and language skills; learning disabilities are common. |
| Triple X Trisomy X | 47,XXX | 1 in every 1000 newborn girls. Tall stature, delayed speech and language skills; learning disabilities are common. |
| Turner Monosomy X | 45,XO | 1 in every 2500 newborn females. Short stature, webbed neck, concave sternum, heart and kidney defects, infertility. |
| Robertson Translocation | 45,XX,21 45,XY,21 | 1 in every 10,000 newborns. Normal—the two copies of chromosome 21 stick together. |

Experiment Overview

The purpose of this activity is to analyze a simulated karyotype, called an ideogram, in order to identify the genetic composition of an individual.

Pre-Lab Questions *(Answer on a separate sheet of paper.)*

1. In human chromosomes, the centromere is located in one of three general locations. Draw and label three different chromosomes to show the three possible centromere positions.
2. Describe the two major genetic abnormalities that may be observed through karyotyping.
3. What is the genetic composition of a normal male?

Materials

Cellophane tape
Karyotype Sheet

Denver System Worksheet
Scissors

Safety Precautions

Although the materials are not considered hazardous, please follow all laboratory safety guidelines. Wash hands thoroughly with soap and water before leaving the laboratory.

Procedure

1. Record the Karyotype Sheet number on the Denver System Worksheet.
2. Count the chromosomes on the Karyotype Sheet to determine the total number of chromosomes and record the results on the Denver System Worksheet.
3. Using scissors, carefully cut out the individual chromosomes on the Karyotype Sheet.
4. Arrange the chromosomes in order of decreasing size, from largest to smallest. (That is how they will be arranged on the Denver System Worksheet.)
5. Use the size, centromere location, and banding pattern on each chromosome to match homologous pairs of chromosomes, and place the matching pairs on the Denver System Worksheet, with the centromere on the line provided and the short *p arm* above the line. *Note:* Refer to Table 1 for the centromere locations on human chromosomes.
6. Tape the chromosomes to the Denver System Worksheet. Answer the question on the Denver System Worksheet.