NAME _____

DATE _____

Disorder Detectives: Examining Human Chromosome Disorders

Overview

You and a partner will take on the role of a cytogeneticist working in a hospital. A case study will be given to you for review, along with a set of patient chromosomes. You and your partner will arrange the chromosomes into a completed karyotype on a prepared board. You will analyze the karyotype and diagnose your patient. Your patient may have one of the many types of recognized chromosomal abnormalities, though normal karyotypes are also represented. Be careful and use your observation skills—things are not always as simple as they seem.

Background

In order to think like a cytogeneticist, here are a few things you will need to know.

What is a chromosome?

The DNA of all living organisms is organized into discrete packets called chromosomes. Most human cells contain 46 chromosomes, grouped into two sets of 23—a maternal set contributed by the mother's egg and a paternal set contributed by the father's sperm. The maternal and paternal chromosomes of a pair are called homologous chromosomes, or homologs. Within each set of chromosomes there is one sex chromosome and 22 other chromosomes, called autosomes. There are two types of sex chromosomes, classified as "X" and "Y." Typically, a male has both an X and a Y chromosome, while a female has two X chromosomes.

What is the structure of a chromosome?

Most of the time, the chromosomes are present as long, tangled chromatin strands composed of DNA tightly wrapped around histone proteins and further condensed and stacked. At this stage, individual chromosomes cannot be distinguished from one another.

During cell division, the DNA is replicated and even further condensed. The two copies of each chromosome, called sister chromatids, are temporarily held together at a specific location on the chromosome called the centromere. At this point, individual chromosomes can be identified.

How are chromosomes classified?

Chromosomes vary in size and shape. Centromere location is another feature used to distinguish one chromosome from another. Metacentric chromosomes have arms of roughly equal lengths. The arms of submetacentric chromosomes are more unequal. It is easier to distinguish the shorter arm, called the p arm, from the longer arm, called the q arm. Acrocentric chromosomes have a centromere that is even closer to one end of the chromosome, making their p arms even shorter in relation to their q arms. At each end of a chromosome is a protective region called a telomere.

When stained with Giemsa stain, different chromosomes have different banding patterns. These patterns of dark and light bands uniquely identify each chromosome. The bands do not indicate genes—for some chromosomal regions, hundreds of genes may be present in one band, while in other regions, there may be relatively few genes per band.

What is a karyotype?

A karyotype is an organized profile of an individual's chromosomes. Generally the chromosomes have been stained, identified, and organized in a specific order. This allows a scientist called a cytogeneticist to examine the chromosomes and quickly identify alterations that may result in a genetic disorder. Chromosomes are typically prepared for karyotyping with the sister chromatids so closely aligned that they appear as a single structure (in other words, they look like an "I" rather than an "X").

What types of samples are often obtained for karyotyping?

Cells may be obtained from various sources for karyotype analysis, including

- blood.
- skin or other tissues.
- chorionic villi (part of the placenta). Chorionic villus sampling (CVS) involves removing some of the chorionic villi so the cells can be analyzed. This test, which can be conducted at 10–13 weeks' gestation, carries a 1–2% risk of miscarriage.
- amniotic fluid. Amniotic fluid surrounds the fetus and contains fetal cells that have been shed. The process of withdrawing this fluid using a hollow needle is called amniocentesis. It is conducted at 14–20 weeks' gestation and carries a 1% or less risk of miscarriage.

Examples of Findings Commonly Identified by Karyotyping

Common Karyotype Findings	Associated Clinical Symptom
9/22 translocation	chronic myelogenous leukemia
5p deletion	cri du chat
22q11.2 deletion	22q11.2 deletion syndrome
trisomy 21	Down syndrome
trisomy 18	Edwards syndrome
XXY	Klinefelter syndrome
46 chromosomes (XX)	typical female
46 chromosomes (XY)	typical male
3p25q21 inversion (1 normal chr. 3, 1 inverted chr. 3)	no clinical symptoms present
9p11q12 inversion (1 normal chr. 9, 1 inverted chr. 9)	no clinical symptoms present
trisomy 13	Patau syndrome
14/21 translocation (1 normal chr 14, 1 chr14/21 translocation, 2 normal chr 21)	Robertsonian translocation–Down syndrome
monosomy X	Turner syndrome
trisomy X	XXX syndrome
XYY	47, XXY male

What benefits are provided by karyotyping?

Prenatally, the results of a karyotype can provide answers or a diagnosis. Parents may utilize this information to identify a care team to be present at the birth or to make an informed reproductive decision. In postnatal cases, the results can be used to diagnose complicated syndromes.

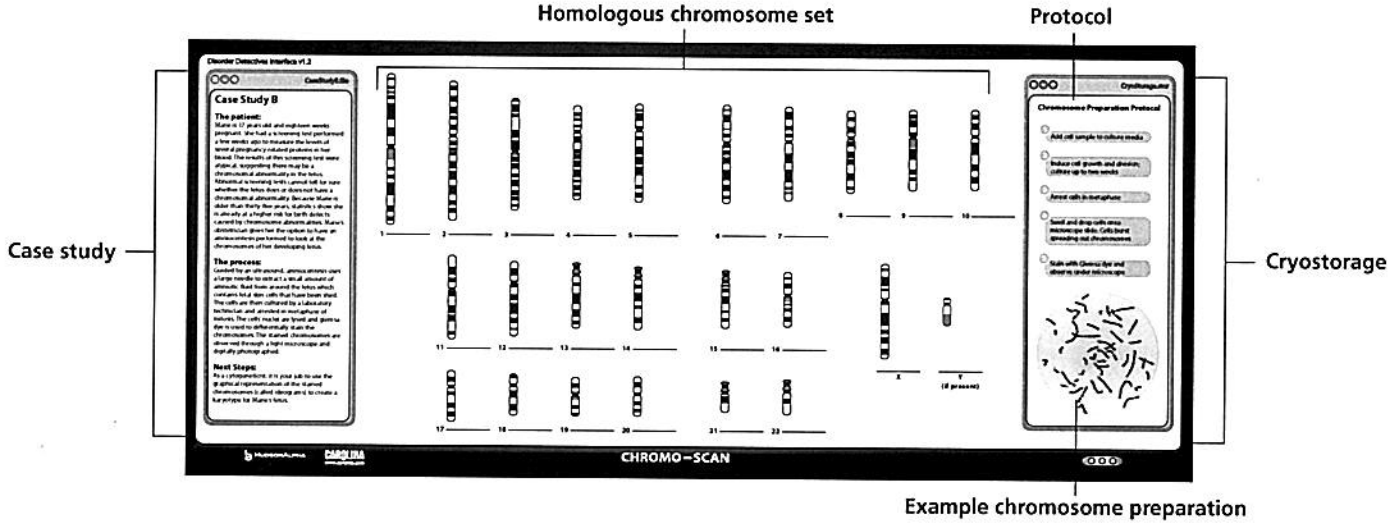
Often a pregnant woman is offered a blood test to help identify certain chromosome disorders. Is this a karyotype?

Pregnant women are offered a screening test for a number of disorders, including neural tube defects and certain chromosomal disorders. Although the word "screening" is often used loosely as a synonym for "testing," the two are not identical and the maternal blood test is not used to create a karyotype for the fetus.

The screening tests measure specific proteins found in the blood of pregnant women to identify who should be offered more extensive (and often more invasive and expensive) testing, such as amniocentesis to obtain fetal cells for karyotyping. The screening test is not 100% sensitive and often women who are carrying a normal fetus have an abnormal screening test and must deal with the stress of deciding whether or not to undergo amniocentesis. At the same time, in a small number of cases, truly abnormal pregnancies go undetected by the maternal blood screen.

Procedure for the Karyotyping Activity

1. Make sure you receive a copy of the "Cytogenetics Report for G-Banded Karyotype" from your teacher.
2. You will also receive a Chromoscan board containing a case study and set of patient chromosomes (reusable decals). Each case study has a Case ID (letters A–O) and a unique color. The color of the patient chromosomes matches the color that is printed around the case study section of the Chromoscan board. Confirm that the colors of the chromosomes and the board match.
3. Select a chromosome decal from the cryostorage area of the board and sketch it on your Cytogenetics Report, noting the centromere, telomere, and p and q arms. Note the centromere position and identify the chromosome as metacentric, submetacentric, or acrocentric.
4. Read the case study found on the left side of the board.
5. On the Cytogenetics Report, record patient information, including name, case ID, reason for referral, patient age, and source of cells.
6. To make the process of karyotype assembly less complex, one of each of the homologous chromosomes is already illustrated on the board. Identify the other homolog and place it on the board in the proper position.
7. Once the karyotype is completed, analyze it for chromosomal anomalies, paying particular attention to chromosome number and structure.
8. Record chromosome number, gender, and chromosomal findings on the Cytogenetics Report.
9. Determine the suggested diagnosis by looking at the table "Examples of Findings Commonly Identified by Karyotyping."
10. Complete the Cytogenetics Report on your patient to include patient diagnosis.
11. Briefly explain on the Cytogenetics Report how a karyotype is prepared. A summary of the technique can be found on the right-hand side of the board where the chromosomes are stored.
12. Discuss the questions found at the bottom of the Cytogenetics Report and write out your answers.
13. At the end of the activity, return the chromosome decals to the cryostorage region of the Chromoscan board **in random order,** to prepare the board for the next group's use. Check carefully around your desks and lab tables to make sure all the chromosomes have been collected and returned to the board.



NAME _____

DATE _____

Cytogenetics Report for G-Banded Karyotype

Select a chromosome from the cryostorage area. Sketch the chromosome, labeling the p arm, q arm, centromere, and telomere.

Chromosome type: _____ metacentric _____ submetacentric _____ acrocentric

Patient Name	Case Study ID	Age
Why is the patient being referred for karyotyping?	Source of Cells for Karyotyping _____ Blood _____ Amniocytes _____ Chorionic Villi _____ Other (specify) _____	
Total Number of Chromosomes Observed	Gender	
Chromosomal Findings _____ no observable chromosomal abnormalities _____ monosomy (chromosome # _____) _____ trisomy (chromosome # _____) _____ deletion (chromosome # _____, arm _____) _____ insertion (chromosome # _____, arm _____) _____ translocation (chromosome #s _____ and _____) _____ inversion (chromosome # _____, arm(s) _____)	Patient Diagnosis	
(Optional) On a separate sheet of paper, attach notes for patient's caregiver with additional implications of the diagnosis, including life expectancy, complications, available treatments, and support group information.		
Briefly explain how a karyotype is prepared.		
Why do you think that relatively few fetuses with chromosomal trisomies survive to birth?		
Why are microdeletions and microinsertions difficult to diagnose using karyotyping?		