

# Karyotyping Cancer Cells

## Introduction

Cancer is a large, overwhelming, and sometimes frightening diagnosis. The concept is to big that we forget that cancer starts small, at the cellular level. How are cancer cells different than normal cells? The purpose of this activity is to analyze a simulated karyotype, called an *ideogram*, in order to identify the genetic composition of both a normal cell and a cancerous cell.

## Concepts

- Cell division
- Chromosomes
- Karyotype
- Mitosis

## Background

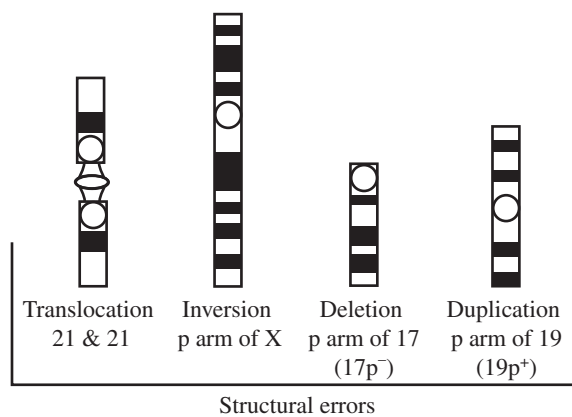
Cell division occurs due to a complex set of cell signals. These cell signals cause the transcription of specific genes, the generation of new organelles, and control the general function of a cell. Built in to cell division are three checkpoints. In eukaryotic cells, these checkpoints are points within cell division in which the cell can go one of three ways: cell division can be halted either temporarily or permanently; cell division can proceed; or cell death can be triggered. These checkpoints have been evolutionarily conserved, meaning the checkpoint mechanisms in fruit flies are very similar to those in our own bodies. At each of the three checkpoints the cell determines whether or not all of the components and conditions have been met for cell division to proceed. Each checkpoint involves numerous molecules interacting in a set of complex cell signaling pathways. A change to these signaling pathways can cause cell division by promoting molecules to be expressed more than usual or by hindering molecules expression. Any of these changes in a normal cell's signaling pathways can cause the cell to replicate out of control—this is cancer.

The cell damage can be from an infection by certain viruses, from a physical source such as UV damage, from a chemical source such as benzene, or by a genetic defect that occurred during the rapid replication of fetal development.

Once the cell is off track, multiple mutations begin to build up, including aneuploidy and structural errors. *Aneuploidy* means that a cell has an abnormal number of chromosomes. *Structural errors* occur when part of a chromosome is missing or not in its correct position. Pathologists and geneticists stain and view a cell's metaphase chromosomes using a light microscope. The stain used to help visualize the chromosomes causes a very specific banding pattern on the chromosome. Any structural changes or additional chromosomes are easily seen using this technique called *karyotyping*.

A typical cell will have 46 chromosomes; any more or less is aneuploidy. If there is a large structural change or error in the chromosome, the banding pattern is altered. There are four types of structural errors—translocations, inversions, deletions, and duplications (see Figure 1). *Translocations* arise when part of one chromosome breaks off and attaches to another chromosome. *Inversions* involve a section of a chromosome breaking off and then reattaching to the same chromosome upside down. A *deletion* is when a section of a chromosome is completely absent. *Duplications* occur when a section of the chromosome is repeated.

An example of a virus that causes cancer is a subtype of the human papillomavirus (HPV) known as HPV-18. HPV-18 is particularly aggressive. Within the virus's 8,000 base pair DNA genome is the code for two checkpoint interfering proteins. Like many viruses, HPV inserts itself into the chromosome of the host cell and the viral proteins are transcribed along with the host proteins. One of the two viral proteins targets a cell division repressor molecule. The first viral protein tags the repressor molecule for destruction by the cell. The second viral protein acts by binding to a host protein, which traps it. This particular host protein is a cell division promoter. By residing in the promoter's inhibition location, the virus causes the cell to move through the checkpoint and into cell division where a normal cell would have halted for repair before proceeding.

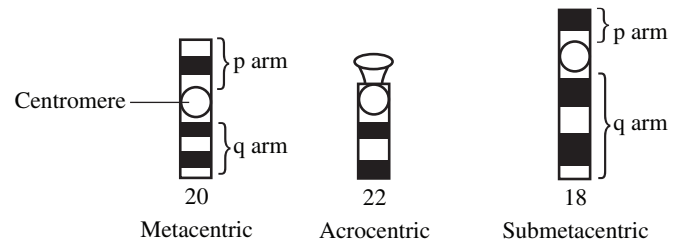


**Figure 1.**

## Karyotyping Cancer Cells *continued*

Chronic myeloid leukemia (CML) is a type of cancer caused by a translocation error. The specific translocation involves the bottom part of chromosome 22 breaking off and attaching to the bottom of chromosome 9 and a small part of the bottom of 9 attaching to the bottom of 22. The abnormally short chromosome 22 is called the Philadelphia chromosome because the idea that this short chromosome 22 was responsible for this disease was first determined in the city of Philadelphia.

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. After staining, each pair of homologous chromosomes is easily distinguished from other chromosomes by differences in length, centromere position, 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 2). 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*. The area above the centromere is called the p arm while the area below the centromere is called the q arm.



**Figure 2.**

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 1).

**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

Matching the bent and twisted shapes of an actual stained chromosome is a daunting task. Ideograms are black and white simulated chromosomes which make karyotyping a faster task for the untrained student. On the next page is a sample ideogram for each autosome, plus X and Y (see Figure 3). The sample ideogram chromosomes in Figure 3 do not show any changes due to structural error.

## Materials

Denver System Worksheet  
 HeLa karyotype  
 Mantle cell lymphoma karyotype t(11;14)  
 Normal female karyotype

Normal male karyotype  
 Philadelphia karyotype t(9;22)  
 Unknown karyotypes

Sample ideograms for each chromosome.

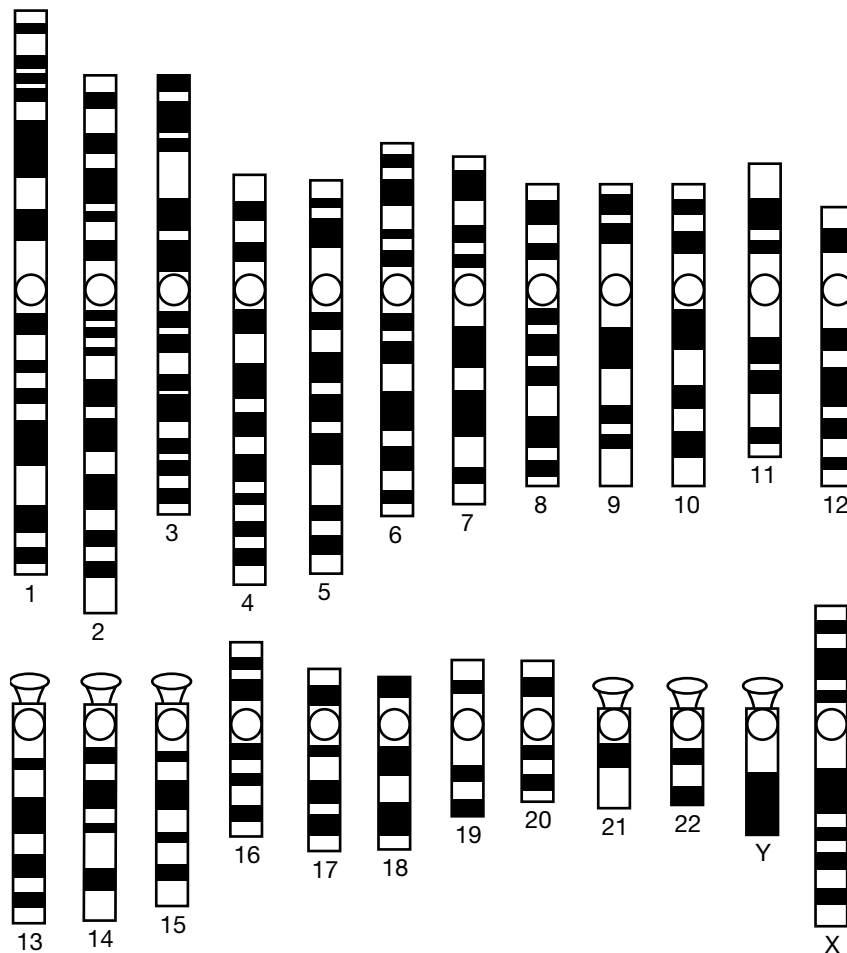


Figure 3.

**Safety Precautions**

The materials used in this activity are considered nonhazardous. Please follow all normal classroom safety guidelines.

**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.
7. Determine which karyotype you analyzed. The choices are listed in the *Materials* section.
8. Some information regarding the three cancer karyotypes was given in the *Background* section. Choose to conduct research on one of these cancers or on another cancer of your choice. Present your finding to your class as a poster, paper or presentation.

### Disposal

The pieces of paper may be disposed of in the normal trash.

### AP Biology Curriculum Framework (2012)

Essential knowledge 3.A.1: DNA, and in some cases RNA, is the primary source of heritable information.

Essential knowledge 3.A.2: In eukaryotes, heritable information is passed to the next generation via processes that include the cell cycle and mitosis or meiosis plus fertilization.

### Tips

- **Answer Karyotype Sheet 1** is a normal female.
- **Answer Karyotype Sheet 2.** The chronic myeloid leukemia karyotype has one extra-long chromosome 9 and one very short chromosome 22. The remainder of the karyotype is that of a normal female.
- **Answer Karyotype Sheet 3** is a normal male.
- **Answer Karyotype Sheet 4**—The mantle cell lymphoma karyotype has one altered chromosome 11 and one altered chromosome 14. The remainder of the karyotype is that of a normal male.
- **Answer Karyotype Sheet 5**—The HeLa karyotype is very different from a normal female karyotype. Chromosomes 3 and Y are absent. Chromosome 22 only has one copy present. Chromosomes 4, 8, 12, 19, and X have 2 copies present. Chromosomes 1, 2, 7, 11, 3, 14, 18, 20, and 21 have 3 copies present. Chromosomes 5, 9, 10, 15, 16, and 17 have 4 copies present. Chromosome 6 has 5 copies present. The HeLa cell line has changed over the last 60+ years. There are so many different variations in chromosome number that the cell line chromosome number is noted as a subscript. For example, the karyotype used for this activity is HeLa<sub>67</sub>. HeLa is a cell infected by HPV-18.
- Chromosome 21 actually contains fewer base pairs, and is therefore shorter, than chromosome 22. This was not known in 1961 when the Denver System was established.
- Fluorescent in situ hybridization (FISH) is the most common staining or banding procedure used by geneticists. There were several different stains used prior to the FISH technique. The most popular old stain technique was G-Banding with Giemsa stain.
- The Philadelphia chromosome was the first direct link between malignancy and a chromosomal abnormality. There are several interesting articles about the discovery of the translocation and the wide range of new research inspired by the discovery.

### References

The Legacy of the Philadelphia chromosome (accessed March 2012).

<http://www.uphs.upenn.edu/news/features/philadelphia-chromosome/>

Genetics Home Reference, a service of the U.S. National Library of Medicine (accessed March 2012) <http://ghr.nlm.nih.gov>

MedlinePlus, a service of the U.S. National Library of Medicine (accessed March 2012) <http://medlineplus.gov/>

### Materials for *Karyotyping Cancer Cells* are available from Flinn Scientific, Inc.

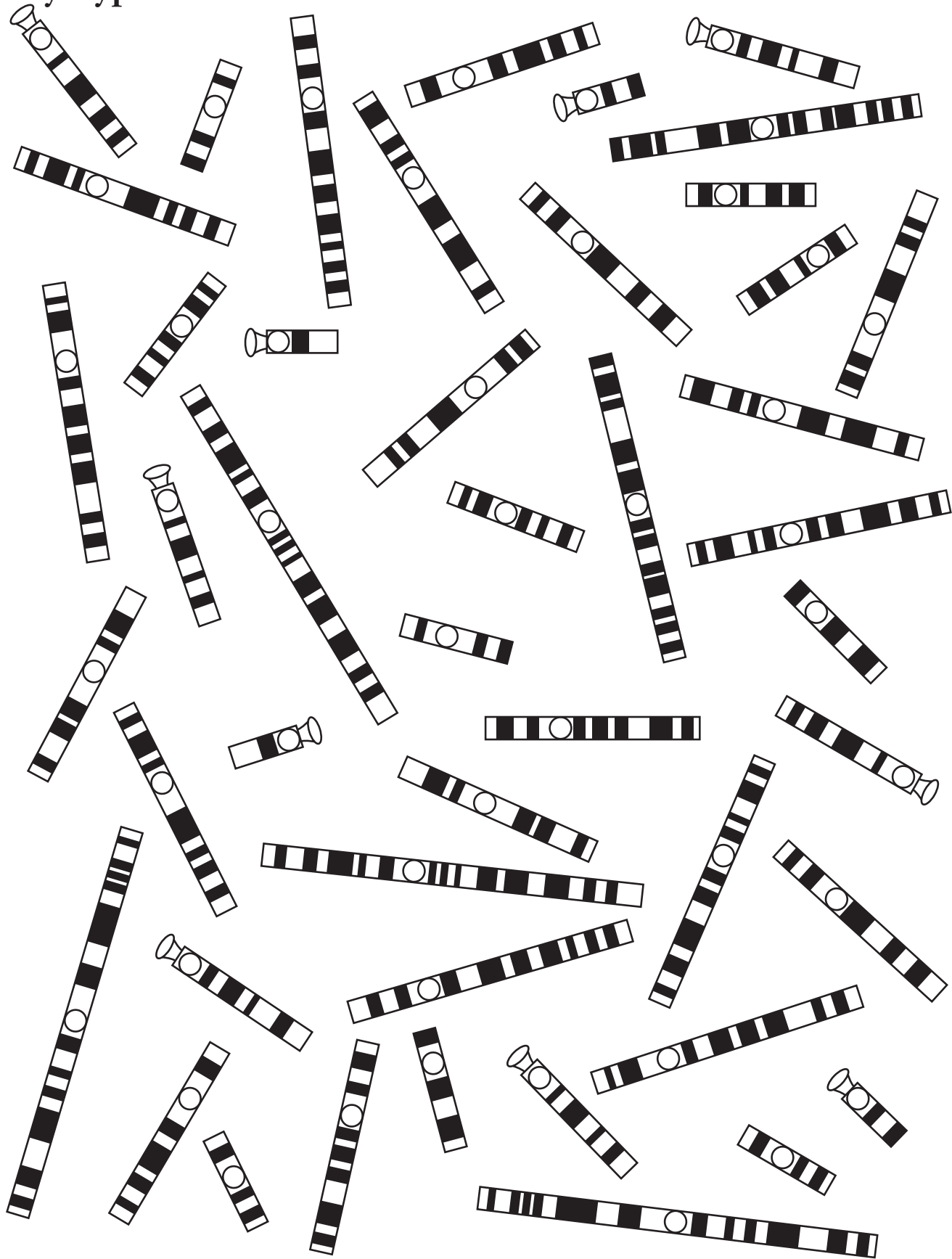
Catalog No.	Description
FB2033	Cancer and the Loss of Cell Cycle Control

Consult your *Flinn Scientific Catalog/Reference Manual* for current prices.



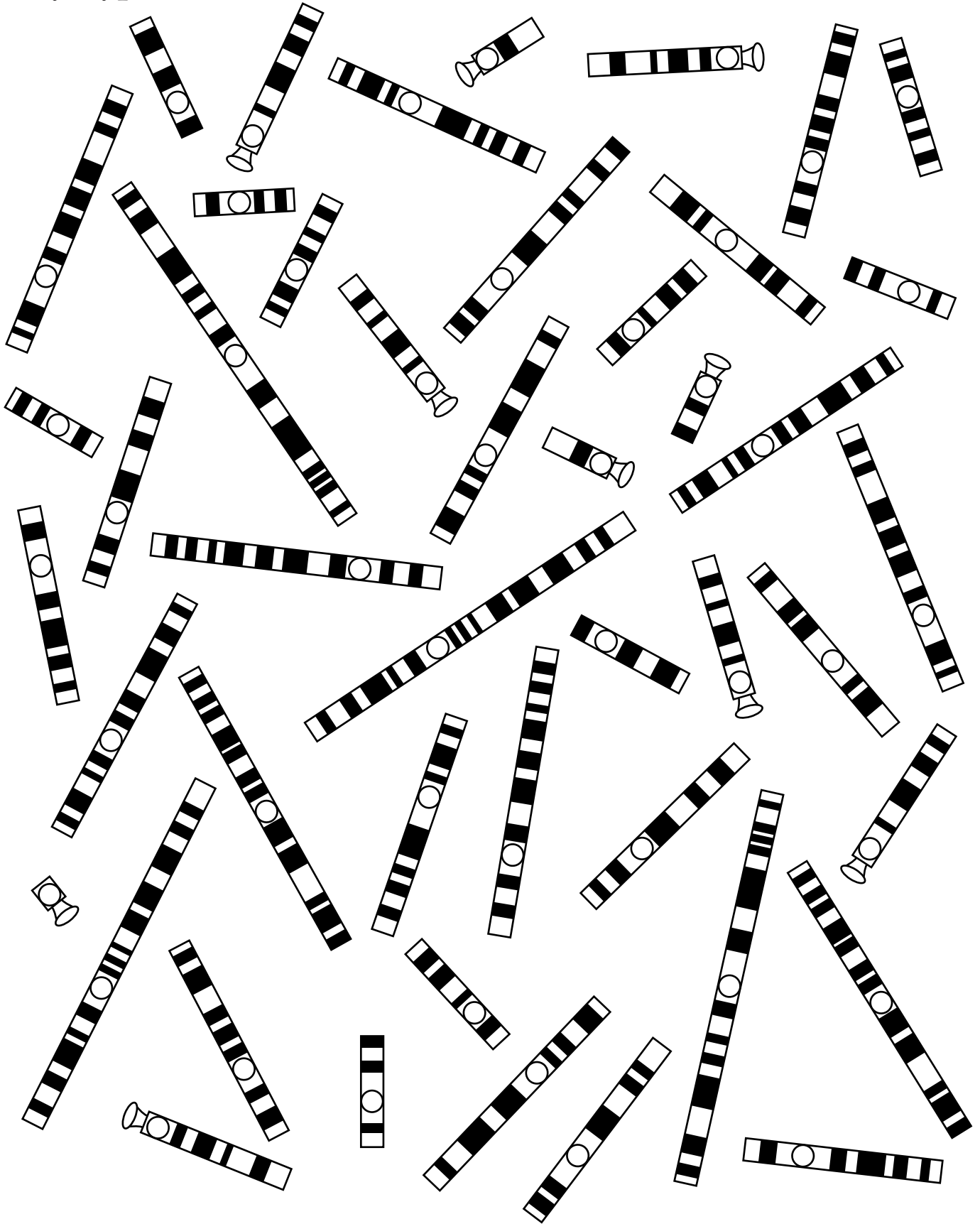
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# Karyotype Sheet #1



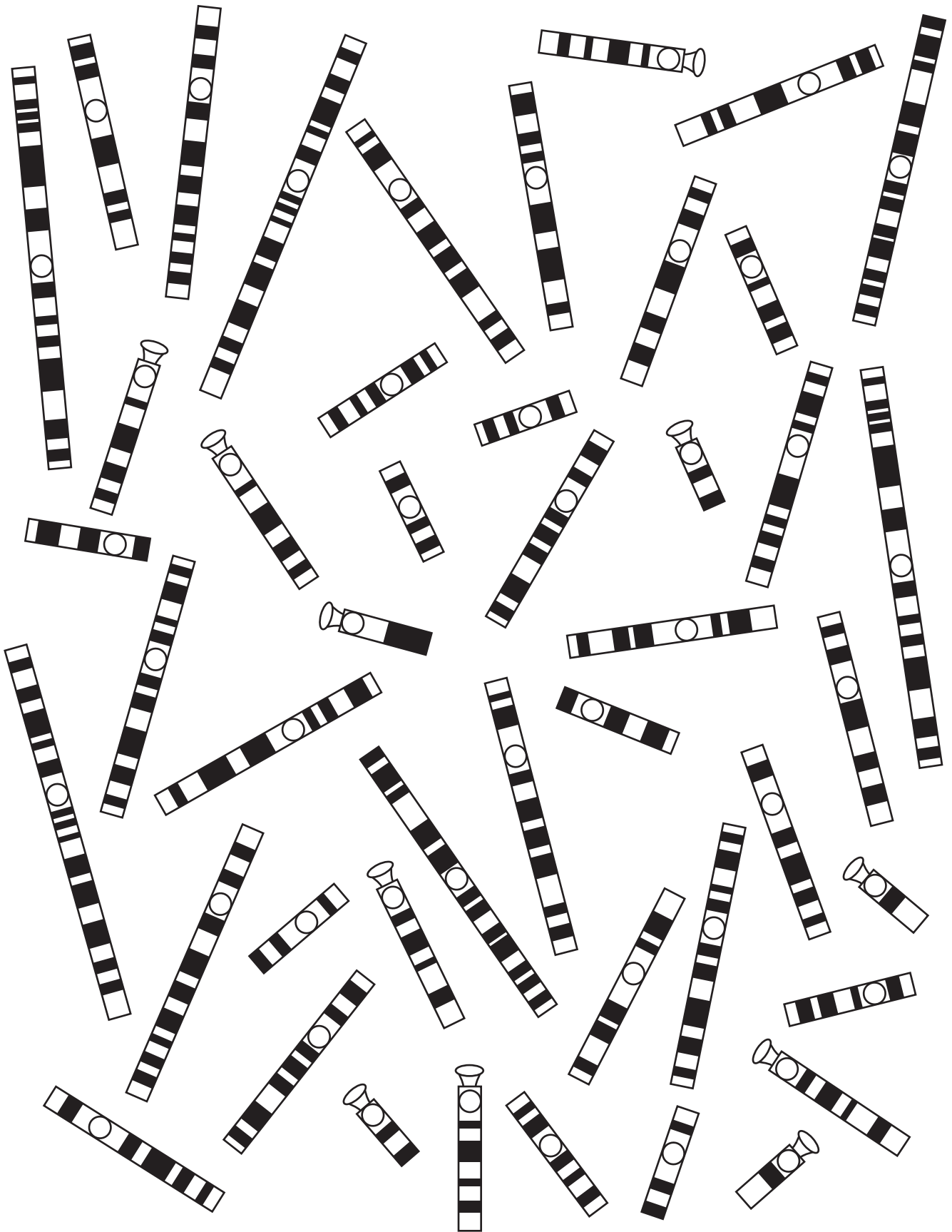
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# Karyotype Sheet #2



Name: \_\_\_\_\_

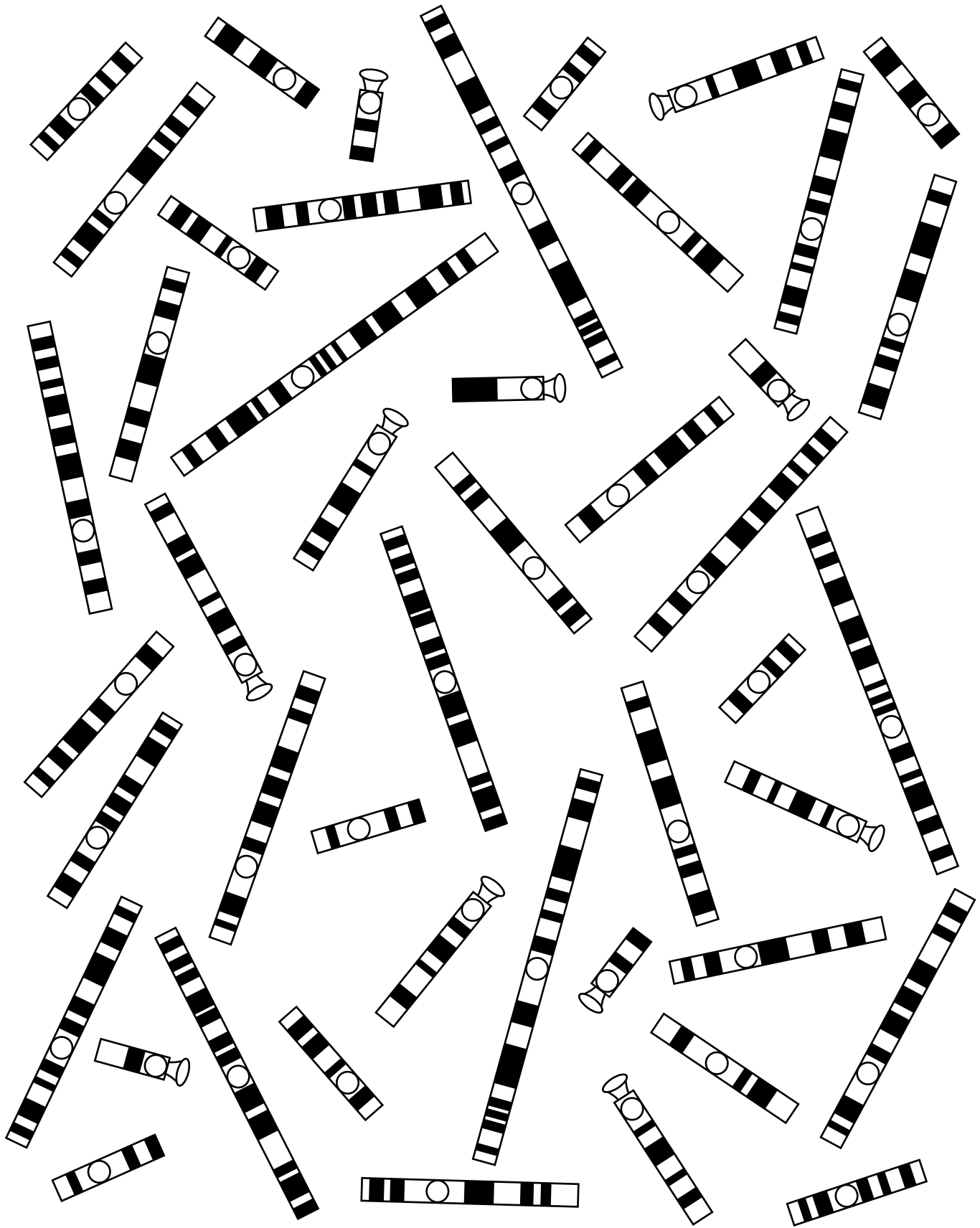
# Karyotype Sheet #3





Name: \_\_\_\_\_

# Karyotype Sheet #4



Name: \_\_\_\_\_

# Karyotype Sheet #5

