HUMAN CHROMOSOME SET

1. Hello! Welcome to the second Module of our course, where we'll talk about the organization of our genetic material.

2. As we discussed in the first lecture of Module 1, Mendel proposed that the two copies of a gene separate from each other during the formation of gametes. We know that these cells, the gametes are produced by a form of cell division called meiosis. Meiosis is the process that reduces the amount of genetic material by one-half. When an egg and sperm fuse at fertilization, the genes from the mother and father become members of a new gene pair in the offspring.

3. In the mid-twentieth century it was discovered that genetic information is housed on DNA and that this molecule is part of cellular structures known as chromosomes. A combination of biochemical, molecular, and microscopic techniques has provided a great deal of information about the organization and structure of chromosomes. In humans each chromosome consists of one double-stranded DNA molecule combined with proteins to form chromatin.

4. Of proteins associated with DNA, the most essential structural role play positively charged histones. The DNA is first coiled around them to form nucleosomes. The nucleosomes are coiled again and again into fibers that form the body of the chromosome. When you look at this model of chromosomal structure, please, keep in mind that chromosomes undergo cycles of coiling and uncoiling in mitosis and interphase, so that their structure is, in fact really very dynamic.

5. A branch of genetics that studies chromosomes and their role in heredity is called cytogenetics. It is one of the most important investigative approaches in human genetics and is used, among other things, to map genes and study chromosome structure and abnormalities. The earlies cytogenetic studies used light microscopy that continues to be useful in clinical settings in preparing karyotypes- standardized arrangements of chromosomes that help to diagnose or rule out certain genetic disorders.

6. Here you see the list of some commonly accepted clinical indications for standard cytogenetic analysis such as karyotyping. These include: any malformations associated with a particular syndrome or aberration, developmental delay, maldefined genitalia (internal or external) that may make determining the child's gender difficult, delayed puberty or inappropriate secondary sexual development, clinically significant abnormal growth, such as: short stature, excessive growth, micro- or macrocephaly, family history of chromosome abnormality, infertility or miscarriages, cancer, and prenatal diagnosis.

7. As it was shown at the beginning of this lecture, human body cells have a diploid nucleus, which contains two copies of each chromosome, in homologous pairs. Humans have a diploid number of 46 chromosomes in 23 pairs. In a karyotype, the chromosomes are arranged systematically in pairs, from longest to shortest, and numbered from 1 (the longest) through 22 to represent the autosomes. The sex chromosomes- X and Y are usually set off at the bottom right.

8. Chromosomes are most conveniently studied in peripheral blood lymphocytes, but almost any growing tissue including bone marrow, cultivated skin fibroblasts or cells from amniotic fluid or chorionic villi can also be used.

9. In this picture karyotype analysis begins with a blood sample. Lymphocytes isolated from peripheral blood are added to the flask with a nutrient growth medium. Because lymphocytes normally do not divide, a mitosis-inducing chemical is added to the flask, and the cells are grown for 2 or 3 days at body temperature in an incubator. At the end of the culture period, when there is a large population of dividing cells, the culture is treated with a drug such as colchicine, which disrupts mitotic spindles and prevents completion of mitosis. This step greatly enriches the population of metaphase cells. Next, the lymphocytes are harvested and treated briefly with a hypotonic solution, which swells the cells and aids in the spreading of chromosomes. The swollen lymphocytes are dropped onto a microscope slide. The impact causes the fragile cells to break open, spreading metaphase chromosomes onto the slide. Now the chromosome preparation can be partially digested with trypsin, an enzyme that enhances banding pattern, and stained. Finally, the preparation is ready for observing, photographing, sorting, and counting the chromosomes.

10. Until about 1970, mitotic chromosomes vied under the light microscope could be distinguished only by their relative sizes and the position of their centromeres, the constricted regions joining the two sister chromatids that make up an X-shaped chromosome.

11. In 1971, a meeting was held in Paris to establish a uniform nomenclature for human chromosome-banding patterns based on G-banding.

12. The schematic diagram representing this standardized numbering system is known as an ideogram. This permits the accurate description of breakpoints in chromosome rearrangements and is useful for describing the location of genes in the chromosomal map. All human chromosomes have 2 arms - a short arm and a long arm - that are separated from each other by the centromere. By international convention, the short arm is termed the "p arm" while the long arm of the chromosome is termed the "q arm." Most arms are divided into two or more regions by prominent bands, and each region is further subdivided according to the number of visible bands. Chromosomal regions and bands are labeled consecutively starting from the centromere out toward the telomeres.

13. In Module 5 of this course you will do an activity in which you will be asked to find the *HFE* gene on a chromosome map. The chromosomal locus of this gene might be written "6p21.3". Because "21" refers to "region 2, band 1" this is read as "two one", not as "twenty-one". So the entire locus is "six p two one point three."