SEX CHROMOSOMES

1. Hi everyone, welcome to the second lecture on human cytogenetics, in which we will take a closer look at human sex chromosomes.

2. The human genome is the complete set of nucleic acid sequence for humans encoded as DNA within 22 autosomes, and 2 sex chromosomes which are all large linear DNA molecules contained within the cell nuclei, plus mitochondrial DNA - a comparatively small, circular DNA molecule present in a few copies in each mitochondrion.

3. Autosomes come in pairs of homologous chromosomes. Homologous chromosomes have the same genes arranged in the same order. So for all of the genes on the autosomes, both males and females have two copies. Sex chromosomes, X and Y, are heteromorphic chromosomes- they have different genes. The sex chromosomes determine a person's sex. Women have two X chromosomes, and men have one X and one Y chromosome. And it is the Y chromosome that determines maleness in humans.

4. But the XY sex determination system is not the only mechanism of sex determination. If you want to learn how sex is determined in other groups of animals- I strongly recommend you watch a short but very informative TED-Ed presentation entitled "Sex Determination: More Complicated Than You Thought". You will find a link to this animation in the supplementary materials for this module.

5. Now, coming back to humans- our gametes carry chromosomes - each parent contributes 22 autosomes and one sex chromosome. All eggs produced by females carry an X chromosome; in males, about half the mature sperm carry an X chromosome and half carry a Y chromosome. Egg and sperm join to make a zygote, which develops into a new offspring. An egg plus an X-containing sperm will make a female offspring, and an egg plus a Y-containing sperm will make a male offspring.

6. Following fertilization, a foetus begins to develop. At first, its sexual organs manifest as a genderless gonad, or sex gland – basically a small, thick ridge of tissue near what will become the abdomen. The "default" sex (i.e., without any other further input) is actually female. If a Y chromosome is present, expression of genes on the Y chromosome causes the indifferent gonad to develop as testis.

7. Studies of structural aberrations of the human Y chromosome revealed that maleness is determined by a testis-determining factor (TDF) located on the short arm of the Y chromosome. TDF indeed turns out to be a single gene called *SRY* (for sex-determining region Y) that has been confirmed as the master-switch to turn on the suite of "male" genes in a developing organism. If this gene is absent, the undifferentiated gonad becomes an ovary and sex differentiation occurs along female lines. If the *SRY* is present, a testis forms.

8. Rare exceptions to the rule that sex determination depends on the presence or absence of the Y chromosome occur in XY females, some of which may have deletions or mutations affecting *SRY*, and XX males, in whom *SRY* has been transferred from the Y to the X by accidental recombination.

9. So, as you can see, a line delineating sex is not so rigid– disorders of sex development can complicate reconciling genetics with gender and sex. The sex of an individual can be defined at several levels: chromosomal sex, gonadal sex, and phenotypic sex. In most cases, all these

definitions are consistent, but in others they are not.
There are some ethical, legal, and social implications associated with sex determination in humans. One of them is the issue of verifying the eligibility of an athlete to compete in a sporting event that is limited to a single sex. If you want to learn more on the subject – go to the paper on intersex controversies in women's Olympics, which you will find in the supplementary materials for this module.

10. We already mentioned here that X and Y chromosomes, unlike homologues autosomes, are heteromorphic they differ in size and gene content. In fact the Y chromosome is considered to be largely blank genetically, lacking almost all genes present on the X chromosome.

11. However, on each end of both X and Y chromosomes, there have been identified so-called pseudoautosomal regions (PARs). They are short regions of homology between the X and Y chromosomes. During meiosis in a male individual, the pseudoautosomal regions of the Y-chromosome pair and exchange genetic material with the pseudoautosomal regions of the X-chromosome. The non-pseudoautosomal portion of the X chromosome(NPX) and male-specific portion of the Y chromosome (MSY) do not recombine with each other.

12. Analysis of Y-specific target sequences on the Y chromosome is a largely effective method for determining the chromosomal sex of an individual. In the movie presented in module 4 of our course, I will outline the use of amelogenin gene as a marker for sex identification in forensics. In humans this gene has two loci: AMELX, located on the distal short arm of the X chromosome and AMELY, located near the centromere of the Y chromosome. Sequence homology of the two is about 90% . However differences between AMELX/AMELY sequence enable sex determination of unknown human samples. If you want to know more- make sure you watch the whole movie from module 4.