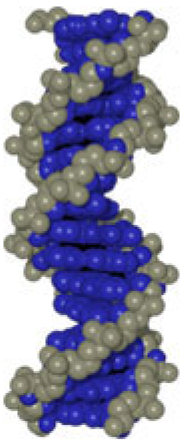

POWERPOINT PRESENTATION NOTES
for
"Gender: In the Genes or in the Jeans? A Case Study on Sexual Differentiation"

by
William J. Hoese, California State University Fullerton
Judith Gibber, Columbia University
Bonnie Wood, University of Maine Presque Isle

These notes accompany the PowerPoint presentation on gonadal and genital differentiation for the "Gender: In the Genes or in the Jeans?" case study by Hoese, Gibber, and Wood. The PowerPoint slides were originally developed as an interactive lecture by Judith Gibber. These slides provide one way for instructors and students to work through the material in Parts III-V of this case. Students work through filling out the various levels of organization as we proceed through the interactive lecture.

Slide 1:

This slide illustrates genetic outcome of sperm containing either an X or a Y chromosome fertilizing an egg with an X chromosome.

Slide 2:

This slide is simply a reminder that the effect of a sperm that contains no sex chromosome results in a zygote that is XO. Zygotes that lack a second sex chromosome develop as females. We can say that genetic sex of the female is determined by the lack of a Y chromosome.

Slide 3:

Slide 3 focuses on the differentiation of the gonads. SRY (present on the Y chromosome) has been shown to code for the protein TDF, testis-determining factor. Under the influence of TDF, Sertoli cells differentiate in the gonadal tissues, followed by Leydig cells, which secrete testosterone. Development of the gonads results from interaction with germ cells that migrate to gonadal tissue. Female differentiation occurs as the default, if no SRY is present.

The presence of SRY and TDF (i.e., chromosomal sex) determines just the gonadal sex of an individual, and this acts as a switch. Products from the gonads provide cues for subsequent differentiation events.

Slide 4:

This slide provides an overview of sexual differentiation with material filled in through the level of the gonads.

Slide 5:

This animated slide depicts the development of the Mullerian ducts and degeneration of the Wolffian ducts in females. It also illustrates the development of the Wolffian ducts and degeneration of the Mullerian ducts in males. These ducts connect the gonads to the outside world. The processes of gonadal differentiation and duct differentiation illustrate two developmental mechanisms. With gonads a single tissue develops in either the male or female direction. With ducts there are two tissues, one develops in the male direction and the other in the female direction. In females, the Mullerian system normally develops into oviduct, uterus, and the upper vagina, while the Wolffian system degenerates. In males, the Wolffian ducts develop into epididymis, vas deferens, and seminal vesicles while the Mullerian system degenerates. In males, the testes secrete Mullerian Inhibiting Hormone (MIH), which causes the Mullerian ducts to degenerate.

Normally one of the ducts regresses in each sex. This occurs at the same time that the indifferent gonad starts to differentiate, so we can ask if the female gonad secretes something that causes the Mullerian duct to develop? If you remove the ovaries from a developing female, the Mullerian system develops and the Wolffian system degenerates. Conclusion based on results is that ovarian secretions are not needed for the Mullerian duct to develop into female system, nor for the Wolffian ducts to regress. Wolffian duct regression may be an example of apoptosis, a kind of cell death that is programmed into the cells.

Slide 6:

We can ask a similar question with males: Does the male gonad secrete something that affects male differentiation?

If you remove the testes from males, then the Mullerian system develops and the Wolffian system degenerates. Conclude that something from the testes causes the Mullerian to regress, and causes the Wolffian to develop. Students may be tempted to say that "testosterone does it," which offers a good chance to point out that we shouldn't draw conclusions beyond the data. The data shows just that the testes are important, we haven't looked at the specific hormone.

Slide 7:

Slide 7 can be used to show which substances influence Wolffian development and Mullerian degeneration. Testes secrete testosterone. How could you tell whether this is the hormone involved in Wolffian differentiation and Mullerian degeneration?

Experiment	**Mullerian**	**Wolffian**
Normal male	-	+
Remove testes	+	-
Remove testes and inject testosterone (T)	+	+
Intact male + anti-testosterone	-	-

The testes must be present for Wolffian ducts to develop, and this can occur without the testes, as long as testosterone (T) is present, so it must be that the testes secrete testosterone, which causes development of the male ducts. The Mullerian ducts regress in a normal male; the testes are needed for this process, because if you remove the testes, the Mullerian ducts don't regress. But testosterone doesn't have an effect! So it must be something else about the testes that causes regression of the Mullerian ducts. This is Mullerian Inhibiting Hormone (MIH).

Slide 8:

Slide 8 presents the overview with duct-level of organization completed (including MIH).

Slide 9:

The animated slide 9 illustrates that undifferentiated genital tissue can develop into either male or female genitals.

Slide 10:

Slide 10 illustrates experiments conducted in the 1930s by Eugen Steinach to determine the cues of genital differentiation. Steinach used guinea pigs in his studies to ask whether external genitals developed as a result of secretions from the gonad. To test this, he removed the gonads from individuals and implanted them with the gonad of the opposite sex. He found that males whose gonads had been removed and replaced with female gonads developed female genitals. He also found that females whose gonads had been removed and replaced with male gonads developed male genitals. He concluded that testis causes male genitals and ovary causes female genitals. But he was missing a crucial control. We ask students to identify this control that Steinach was missing.

Slide 11:

Slide 11 includes the control experiments for determining the cues of genital differentiation. Students discuss Steinach's experiments and realize that he didn't have an experiment where he JUST removed the gonads, WITHOUT adding the gonad of the other sex. These control experiments were done by Jost about 20 years later, and results have been added to this slide. Students discuss what they would conclude from these results.

This animated slide shows the results of these experiments and students conclude that female is the default. In males, the presence of testes induces male genital development. Students can then consider what would happen if a female was injected with testosterone. She would develop male genitals.

Slide 12:

This slide builds to illustrate that signals from the testes are necessary for male genital differentiation.

Slide 13:

Slide 13 builds and reviews differentiation from the chromosomes through the genitals. At this point in the interactive lecture, the chart of differentiation is largely complete. The discussion can turn to the fact that the experiments, thus far, have all been done with laboratory animals. It is not ethical to do these experiments on people, but there are "experiments of nature" that help us conclude that the situation is similar in humans. For example, in very rare cases, a woman develops a testosterone-secreting tumor during pregnancy that results in her XX offspring being born with male genitals.

Slide 14:

This slide illustrates that the female pathway is the default. Without a Y chromosome the genital sex is female. In the absence of SRY and TDF, an ovary develops. In the absence of testosterone and Mullerian Inhibiting Hormone, the Mullerian duct system develops while the Wolffian duct system degenerates. In the absence of testosterone, the female genitalia develop.

Slide 15:

Slide 15 shows that the conversion of testosterone to di-hydroxytestosterone (DHT) is necessary for normal differentiation of the penis. Individuals with 5-alpha reductase deficiency develop along the male pathway up to the genitals, but at birth they have genitals of intermediate form.

Slide 16:

In our case, Terry has XY chromosomes and had testes when she was born. Thus, she had some male characteristics. Terry also has external female external genitals. So, at this point we still need a mechanism that would account for her phenotype.

Slide 17:

In Terry's situation, testosterone is produced by the testes, but for some reason the body can't respond to it. In our classes, students have been introduced to hormone receptors in previous classes so they come up with it easily, but this would be the place to introduce the concept otherwise. Male-typical hormones are produced, but since the receptors for these hormones are absent (or unable to bind the hormone), they are unable to transmit the signals for male genital development. Thus, Terry has a female phenotype.

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