

The Meaning of Sex: Genes and Gender
2001 Holiday Lectures on Science
Chapter List

Lecture One

Deciphering the Language of Sex

David C. Page, M.D.

1. Start of Lecture One
2. Introduction by HHMI President Dr. Thomas Cech
3. Introductory interview with Dr. David Page
4. What was the first thing your parents asked about you?
5. Characteristics of male and female
6. Electron micrograph of egg and sperm
7. Embryonic development and the role of gonads
8. Sex determination can't be explained by the historical idea that heredity is a blending process
9. Historical ideas on environmental factors affecting sex determination
10. Early-20th-century scientists find sex chromosomes in insects
11. What might the sex-determining signal be?
12. Sex of fruit flies linked to number of X chromosomes in 1916
13. Discovery of how sex chromosomes operate in humans
14. XX males and XY females suggest key genes for sex determination
15. *SRY*, the sex-determining gene, in transgenic mice
16. Student question: What are the symptoms of Turner and Klinefelter syndromes?
17. Student question: What causes hermaphroditism in humans?
18. Student question: Why don't XX males produce sperm?
19. Student question: What makes XY females develop as female?
20. Student question: Does *SRY* determine whether a person has testes?
21. Student question: Can Y-chromosome activity be clearly observed in the human body?
22. Student question: Do XY females have male levels of testosterone?
23. Why does nature have two sexes? Are males really necessary?
24. Description of clonal reproduction
25. Comparing cloning in Laredo striped whiptail with sexual reproduction in related species
26. Meiosis is the defining feature of sexual reproduction
27. Is sex, in an evolutionary sense, good?
28. Demonstration: Fresh fruit and rotting vegetables
29. Demonstration: Fruit and vegetables with mutations
30. Demonstration: Meiosis can weed out rotten genes
31. Animation: Meiosis
32. Animation: Picture sequence of human embryonic development
33. Animation: How does an X chromosome gain the *SRY* gene?
34. Student question: With a recessive mutation, would a clonal reproducer be better off?
35. Student question: Is lizard cloning the same as cloning in Dolly the sheep?
36. Closing remarks by HHMI President Dr. Thomas Cech

Lecture Two

Hermaphrodites: The Safer Sex

Barbara J. Meyer, Ph.D.

1. Start of Lecture Two
2. Introduction by HHMI Vice President Dr. Peter Bruns
3. Introductory interview with Dr. Barbara Meyer
4. Why do we study model organisms?
5. Introduction to the nematode *Caenorhabditis elegans*
6. Anatomy of *C. elegans*: every cell is known
7. *C. elegans* has two sexes: male and hermaphrodite
8. Video: *C. elegans* mating
9. *C. elegans* sperm
10. Video: Amoeboid sperm of *C. elegans*
11. A behavior gene in *C. elegans* is related to a human gene important in kidney function
12. Life cycle of a hermaphrodite
13. Fertilization mechanism in *C. elegans*
14. Early embryonic development of *C. elegans*
15. Video: From fertilization to egg laying in *C. elegans*
16. Using mutations to study sex determination in *C. elegans*
17. Activation of sex-determining gene
18. Student question: Why can't human hermaphrodites self-fertilize?
19. Student question: Why aren't there any female worms?
20. Student question: Do hermaphrodites use male sperm preferentially?
21. Student question: Do male sperm permanently displace hermaphrodite sperm?
22. Student question: Did hermaphrodites evolve from females?
23. Student question: Can hermaphrodites mate with each other?
24. Student question: At what stage can you determine the sex of the worm?
25. The basis for sex determination in *C. elegans*
26. Activity of *xol-1* sex-determining gene is dependent on the ratio of X chromosomes to autosomes
27. The balance of X signal elements (XSEs) and autosomal proteins regulates *xol-1* activity
28. Demonstration: Balance of molecules in XO
29. Demonstration: Balance of molecules in XX
30. Demonstration: Balance of molecules in XX with lower levels of XSEs
31. Demonstration: Balance of molecules in XX with much lower levels of XSEs
32. Review of the central dogma of genetics
33. An X signal element (XSE) represses transcription of *xol-1*
34. An XSE also acts to prevent proper splicing of *xol-1* mRNA transcript
35. Summary of repression mechanisms of *xol-1*
36. Does *xol-1* at low levels have any functions?
37. Student question: What is the purpose of the low level of *xol-1* in hermaphrodites?
38. Student question: Is *xol-1* comparable to *SRY* in mammals?
39. Student question: What is the difference between the blue and yellow XSEs in the demo?
40. Student question: What do we know about human hermaphrodites?
41. Student question: Is it possible to produce a worm that lacks *xol-1*?
42. Student question: Do all organisms require a gene to be switched on for male development?
43. Student question: Can you add *xol-1* to a hermaphrodite and make it male?
44. Closing remarks by HHMI Vice President Dr. Peter Bruns

Lecture Three

Sex and Death: Too Much of a Good Thing

Barbara J. Meyer, Ph.D.

1. Start of Lecture Three
2. Introduction by HHMI President Dr. Thomas Cech
3. Introductory interview with Dr. Barbara Meyer
4. Too many chromosomes: Down Syndrome
5. How humans deal with having too many X chromosomes
6. How the nematode deals with having too many X chromosomes
7. *Dumpy (DPY)* gene, a dosage-compensation mutant
8. The *sd*c gene affects both dosage compensation and sex determination
9. Demonstration: Branched pathway for dosage compensation and sex determination
10. Demonstration: The *sd*c gene is turned on in normal hermaphrodite development
11. Demonstration: An *sd*c-mutant hermaphrodite develops as a male without dosage compensation
12. Demonstration: Block sex-determination branch only
13. Demonstration: Block dosage-compensation branch only
14. How does SDC protein interact with the X chromosome
15. How does the male X chromosome avoid dosage compensation?
16. What happens in an *xol-1* mutant?
17. How can you keep an *xol-1* mutant from dying?
18. How can you manipulate *xol-1* mutants to become male?
19. Student question: How do you get a 50% reduction in gene activity?
20. Student question: Does dosage compensation occur on autosomes?
21. Student question: Can a nematode get Down syndrome?
22. Student question: How can Turner syndrome have effects if X inactivation occurs?
23. Student question: What happens in XXX nematodes?
24. Student question: What actually kills when there is no dosage compensation?
25. Student question: How do genes in X chromosomes escape inactivation?
26. Student question: Do autosomes have genes that determine sex?
27. Topics to be covered in the second half of the lecture
28. Review of mitotic chromosome segregation
29. Dosage-compensation proteins evolved from mitotic proteins
30. MIX-1 protein has roles in both mitosis and dosage compensation
31. How does MIX-1 carry out these two roles and not get confused?
32. Where and when is SMC-4 protein found?
33. SMC-4 is only expressed in mitotic cells
34. Video: Embryonic cell division in wild type and SMC-4 mutant
35. Animation: SMC-4/MIX-1 protein in mitosis
36. Animation: SDC/MIX-1 and SMC-4/MIX-1 proteins in dosage compensation and mitosis
37. DPY-28 protein is involved in meiosis
38. Summary of Lecture Three
39. Student question: Can you tag SMC-4 and use it as a marker for mitosis?
40. Student question: At what developmental stage does dosage compensation start?
41. Student question: Is the dosage-compensation mechanism similar to cell division in any way?
42. Student question: How does DPY-28 control the number of crossing-overs?
43. Student question: Without SMC-4, would the chromosome stay tangled?
44. Closing remarks by HHMI President Dr. Thomas Cech

Lecture Four
Sexual Evolution: From X to Y
David C. Page, M.D.

1. Start of Lecture Four
2. Introduction by HHMI Program Director Dr. Dennis Liu
3. Introductory interview with Dr. David Page
4. Description of study measuring testosterone levels of participating students
5. Testosterone study: Student predictions
6. Testosterone study: Interpretations
7. What does the Y chromosome do?
8. Cartoon map of Y-chromosome genes
9. Real map of the Y chromosome: Non-recombining region is passed down clonally
10. Map of the Y chromosome with its three classes of genes
11. Overview of 300 million years of Y-chromosome evolution
12. Synopsis of the animation on Y-chromosome evolution
13. Animation: *SRY* gene evolves and an autosome becomes a Y chromosome
14. Animation: Y chromosome degrades over time
15. Animation: Y chromosome also gains new genes
16. Student question: Why doesn't inversion occur on other chromosomes?
17. Student question: How does temperature determine the sex of a reptile?
18. Student question: Why doesn't the X chromosome undergo inversions?
19. Deletions on the Y chromosome are a leading cause of male infertility
20. Video: Sperm motility in normal- and low-sperm-count samples
21. Some men with low sperm counts are missing part of the Y chromosome
22. Review of spermatogenesis
23. Seminiferous tubules of men with out the *DAZ* gene
24. Intracytoplasmic sperm injection (ICSI) as a remedy for low sperm count
25. Video: ICSI procedure
26. Problem with ICSI and male babies
27. Ethical issues with ICSI
28. Student question: Does ICSI always work?
29. Student question: Does my dog have more genes on its Y chromosome than my brother has?
30. Student question: In ICSI, how is the embryo returned to the uterus?
31. Student question: Will evolution lead to the complete destruction of the Y chromosome?
32. Student question: Will Y-chromosome deletions always be transmitted?
33. Student question: Could we program the sex of a would-be child?
34. Student question: What is considered a normal sperm count?
35. Student question: Why do flies have the Y chromosome but reptiles don't?
36. Student question: Could we reinsert *DAZ* genes in sperm with *DAZ* deletions?
37. Closing remarks by HHMI President Dr. Thomas Cech