ANSWERS TO Problem set questions from Final Exam – Human Genetics, Nondisjunction, and Cancer

Mapping in humans using SSRs and LOD scores

1. You set out to genetically map the locus for color blindness with respect to SSR markers.

(a)

(b) $\log \dfrac{(1/2)\,(0.4)^8\,(0.1)^2 + (1/2)\,(0.4)^2\,(0.1)^8}{(0.25)^{10}}$

(c)

(d) $\log \dfrac{(1/2)\,(0.4)^9\,(0.1)^1 + (1/2)\,(0.4)^1\,(0.1)^9}{(0.25)^{10}}$

2. You are conducting genetic linkage studies to search for a locus (whose chromosomal location has not been firmly established) associated with an autosomal recessive disease.

(a) $\log \dfrac{(1/2)\,(0.49)^4\,(0.01)^0 + (1/2)\,(0.49)^0\,(0.01)^4}{(0.25)^4} = 0.87$

(b) $\log \dfrac{(1/2)\,(0.49)^4\,(0.01)^0 + (1/2)\,(0.49)^0\,(0.01)^4}{(0.25)^4} = 0.87$

(c) $\log \dfrac{(1/2)\,(0.49)^4\,(0.01)^0 + (1/2)\,(0.49)^0\,(0.01)^4}{(0.25)^4} = 0.87$

(d) $\log \dfrac{(1/2)\,(0.49)^3\,(0.01)^1 + (1/2)\,(0.49)^1\,(0.01)^3}{(0.25)^4} = -0.82$

(e) $2 * \log \dfrac{(1/2)\,(0.49)^4\,(0.01)^0 + (1/2)\,(0.49)^0\,(0.01)^4}{(0.25)^4} = 2*(0.87) = 1.74$

(f) LOD = 0.87 + (-0.82) = 0.05

(g) no
(h) yes
(i) yes
(j) no conclusions can be made that are publishable (LOD score > 3)

3. Childhood deafness is often hereditary.
(a) autosomal recessive
(b) the mating of these two people is like a human complementation test – they had mutations in two different genes
(c) no

4. Your colleague, a human geneticist, is conducting genetic linkage studies on the locus associated with an autosomal dominant disease.
(a) negative infinity (there is a recombinant child and thus the two loci cannot be linked at theta = 0)
(b) negative infinity

(c) $\log \dfrac{(1/2)\,(0.5)^4\,(0.00)^1 + (1/2)\,(0.5)^0\,(0.00)^4}{(0.25)^4} = 0.903$

(d) $2 * \log \dfrac{(1/2)\,(0.5)^4\,(0.00)^1 + (1/2)\,(0.5)^0\,(0.00)^4}{(0.25)^4} = 2*(0.903) = 1.806$

5. As we have discussed in class, SSR-based genetic linkage studies in human families can be used to chromosomally localize the loci associated with heritable traits, including diseases.

(a) $\log \dfrac{(0.05)^1\,(0.45)^4}{(0.25)^5} + \log \dfrac{(0.05)^1\,(0.45)^4}{(0.25)^5} = 0.644$

(b) $\theta = 0.2$

$\text{LOD} = 2 * \log \dfrac{(0.1)^1\,(0.4)^4}{(0.25)^5} = 0.837$

(c) 20 cM

6. You are studying a mutation that causes an autosomal recessive phenotype of blindness in humans.

(a) you can't tell which of the genes encodes this mRNA because you don't know how much of the DNA length of each gene is introns, and thus wouldn't be included in the final mRNA transcript

(b) DNA sequencing – find a gene by sequencing in this region that is wild-type in all 10 individuals with normal vision, but is mutated in all 10 who are blind

Calculating Phenotypic concordance using twin studies

1. Congenital pyloric stenosis (an obstruction to the stomach's outlet to the small intestine) has a population incidence of 0.5% in newborn boys and of 0.1% in newborn girls.
(a) possibility #2, because if #1 were correct then girls should have been affected much much less often than boys
(b) no
(c) yes there is a genetic component, it appears that two genes are involved, and there is also an environmental component
(d) because these offspring developed in the womb of a mother who was affected, so the womb environment (such as the mother's hormones) influenced the development of the fetus

2. What phenotypic concordance rates (approximate answers will suffice) might you expect in MZ twins, DZ twins, and first cousins for each of the following diseases?
(a) Chicken pox:
MZ – 100%
DZ— 100%
1st cousins – about the same as unrelated people, but depending on the amount of time 1st cousins spend with each other

(b) Tay-Sachs disease:
MZ – 100%
DZ— 25%
1st cousins – 0%

(c) An autosomal dominant trait in which environment and a single gene are determinants:
MZ – 80%
DZ— 40%
1st cousins – 10%

Meiosis and chromosome loss/gain by non-disjunction

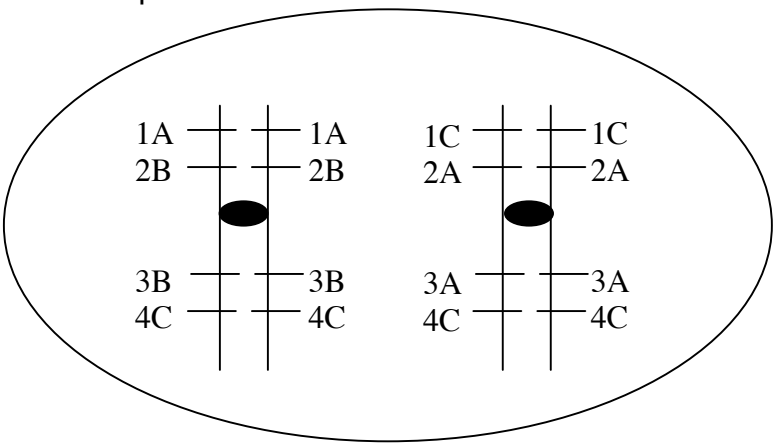
1. While working as a medical geneticist, you encounter an unusual patient: a 47,XXY girl.

(a) mother

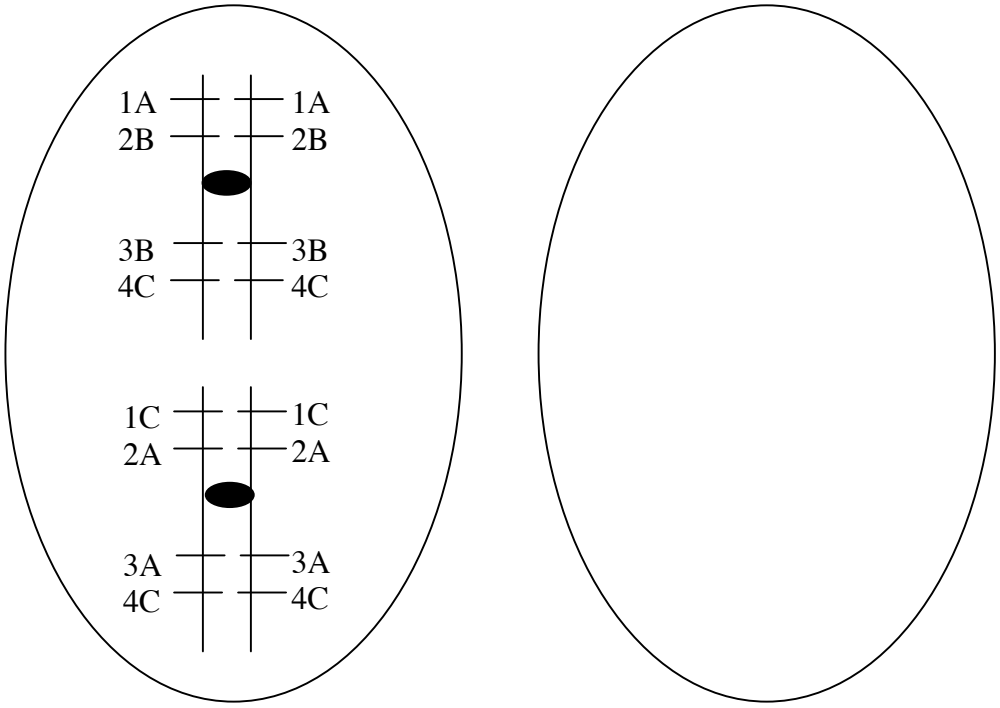
(b) meiosis I

(c)

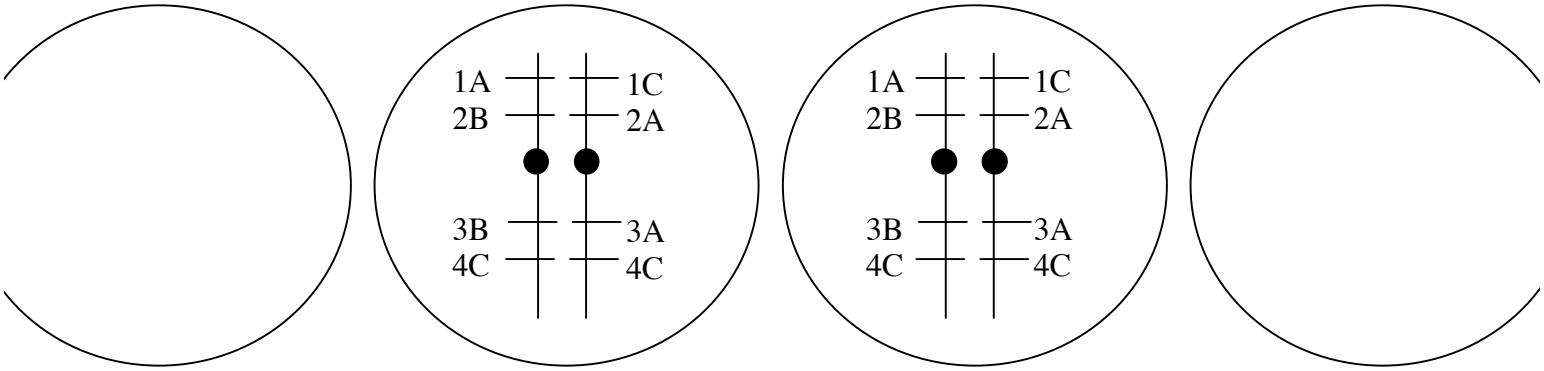
i) the cell in metaphase I



ii) the two cells in metaphase II

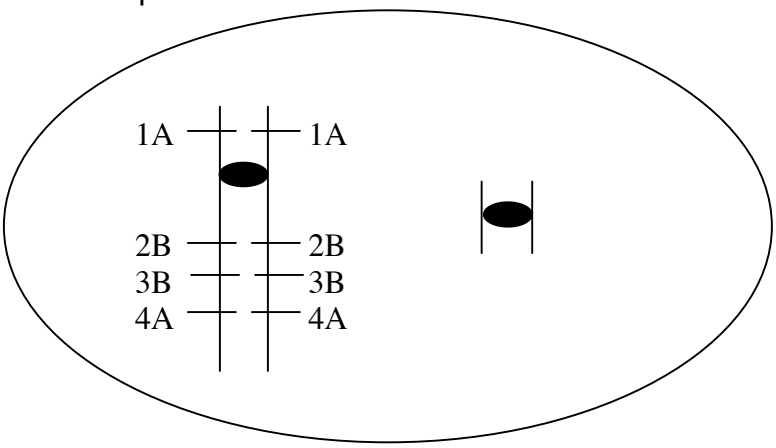


iii) the four final products of the meiosis ✻

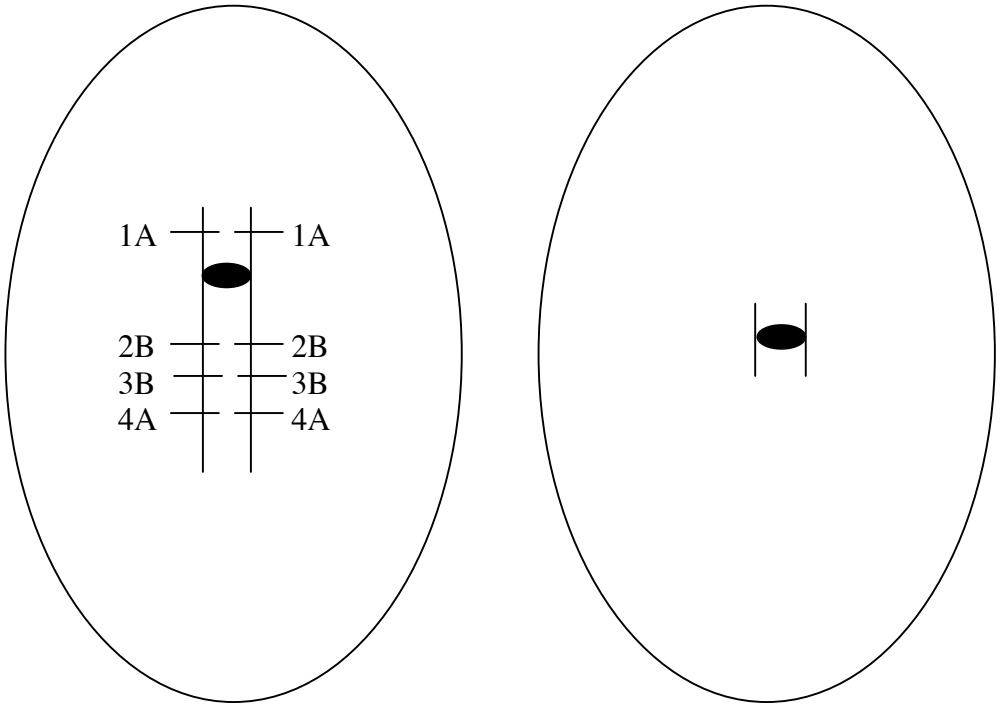


(d) a deletion of the Sry gene
(e) the father had a translocation between the X and Y chromosomes such that the X chromosome carried Sry and the Y chromosome carried SSR1
(f) in the father, during meiosis II

2. Trisomy X (that is, XXX) is one of the most common trisomies observed in human populations.
(a) father
(b) meiosis II
(c)
i) the cell in metaphase I



ii) the two cells in metaphase II



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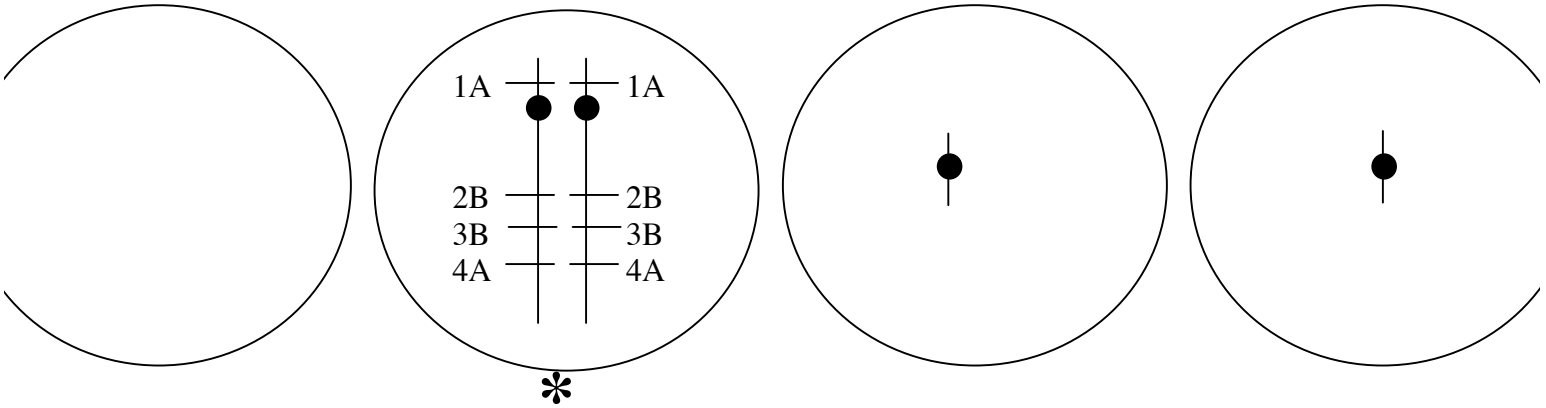
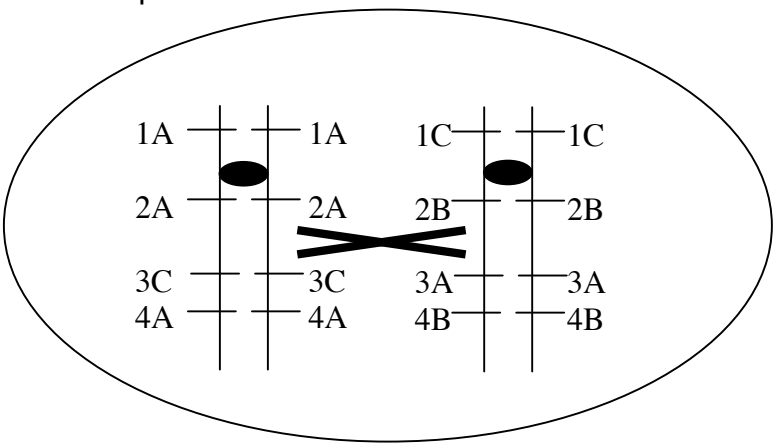


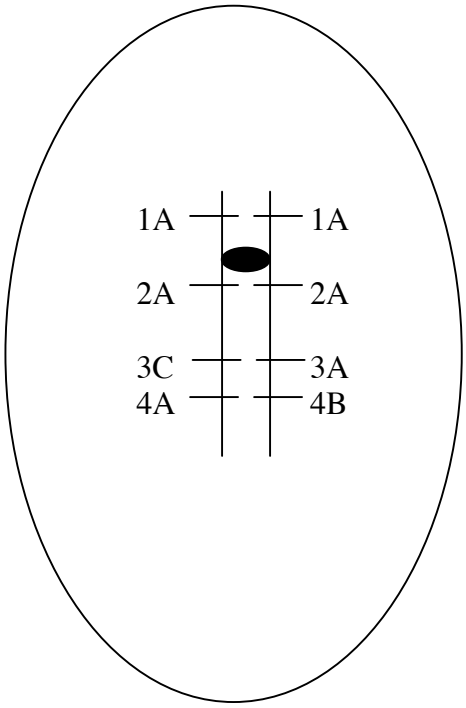
(d) mother
(e) meiosis II

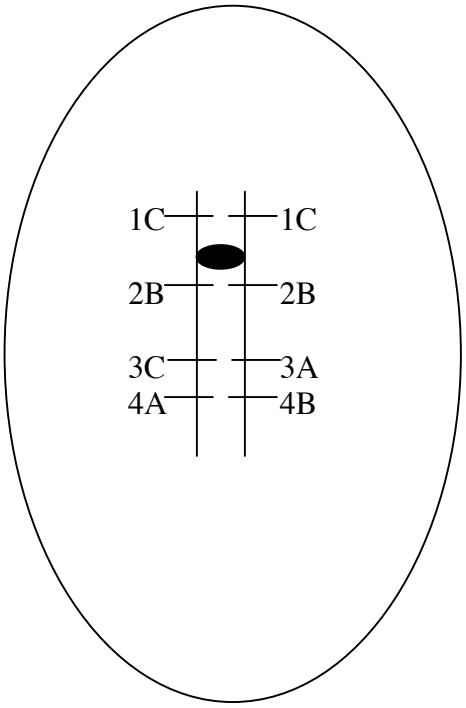
(f)

i) the cell in metaphase I



ii) the two cells in metaphase II





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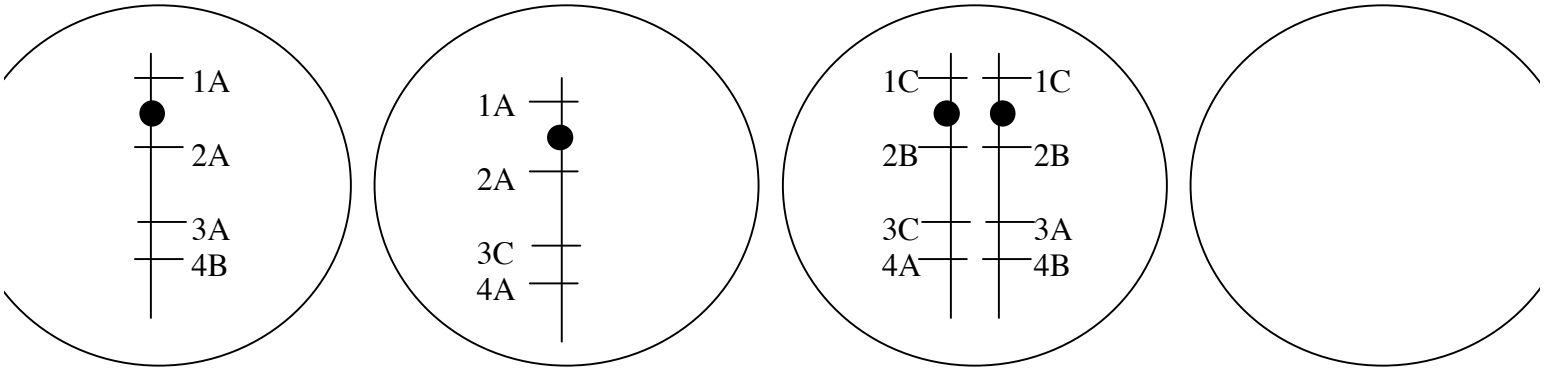

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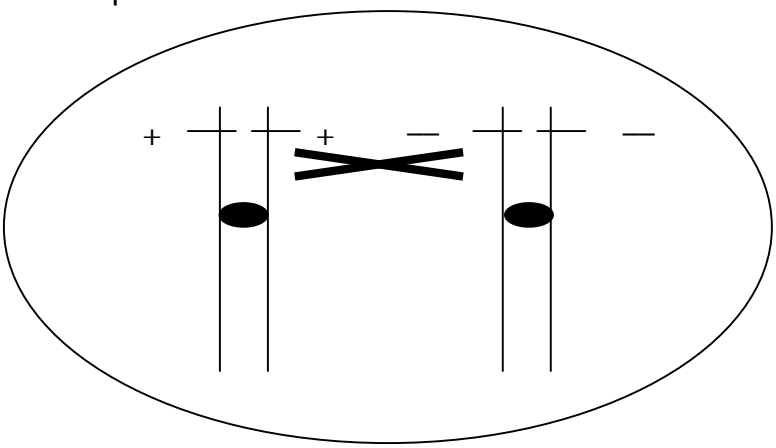
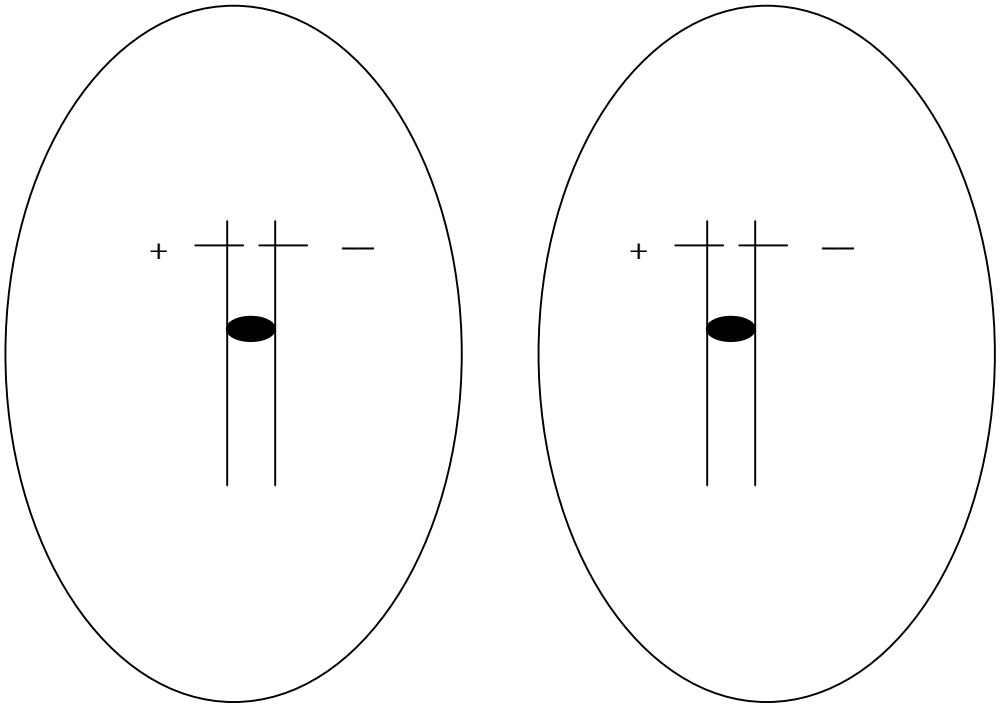
3. A married couple who already had a child with cystic fibrosis approach you because they wish to have another child, but only if they can be assured that the child will not have cystic fibrosis.

(a) recombination

the cell in metaphase I:

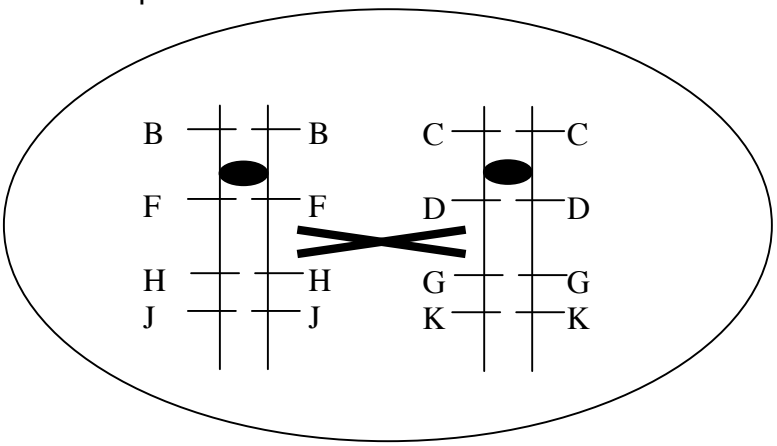


ii) the two cells in metaphase II: THE POLAR BODY

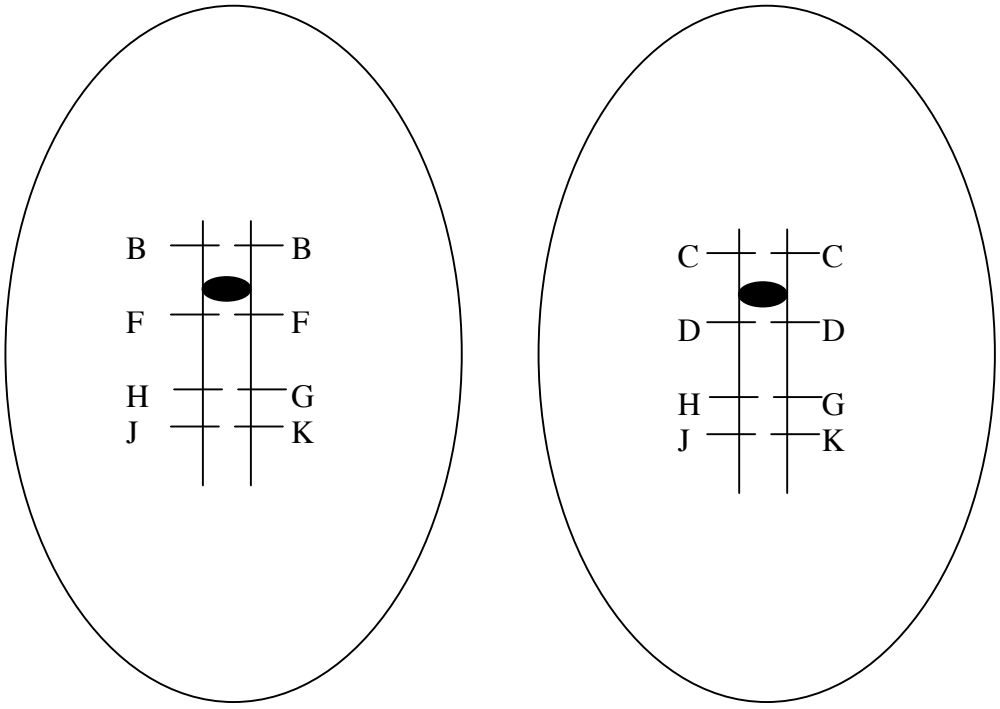


(b) 2 or 3, because the remaining diploid cell that is about to undergo meiosis II only has wild-type copies of the gene
(c) 1 or 5, because then you can test the second polar body to see if it has the deletion, and, if it does, then you know that the oocyte has the wild-type allele

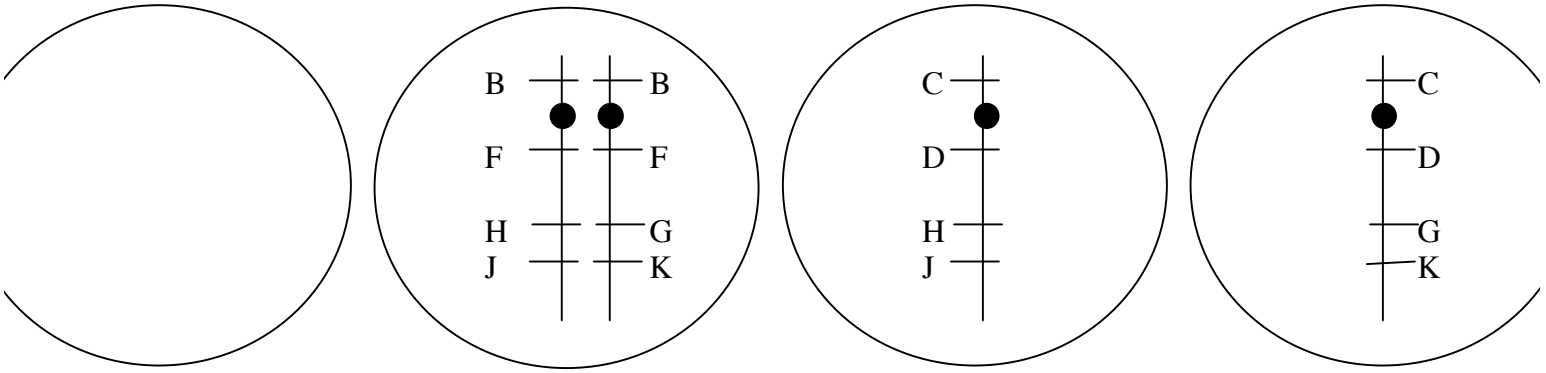
4. Trisomy 18 is one of the most common trisomies observed in human populations.
(a) mother
(b) meiosis II
(c)
i) the cell in metaphase I



ii) the two cells in metaphase II



iii) the four final products of the meiosis



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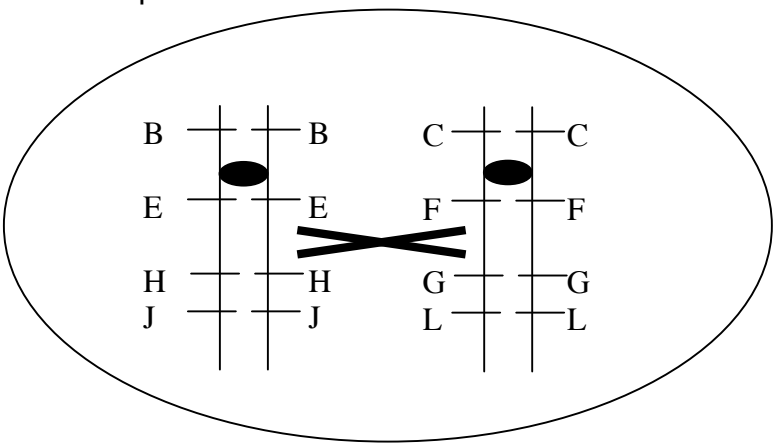
(d) father
(e) meiosis I

(f)

i) the cell in metaphase I



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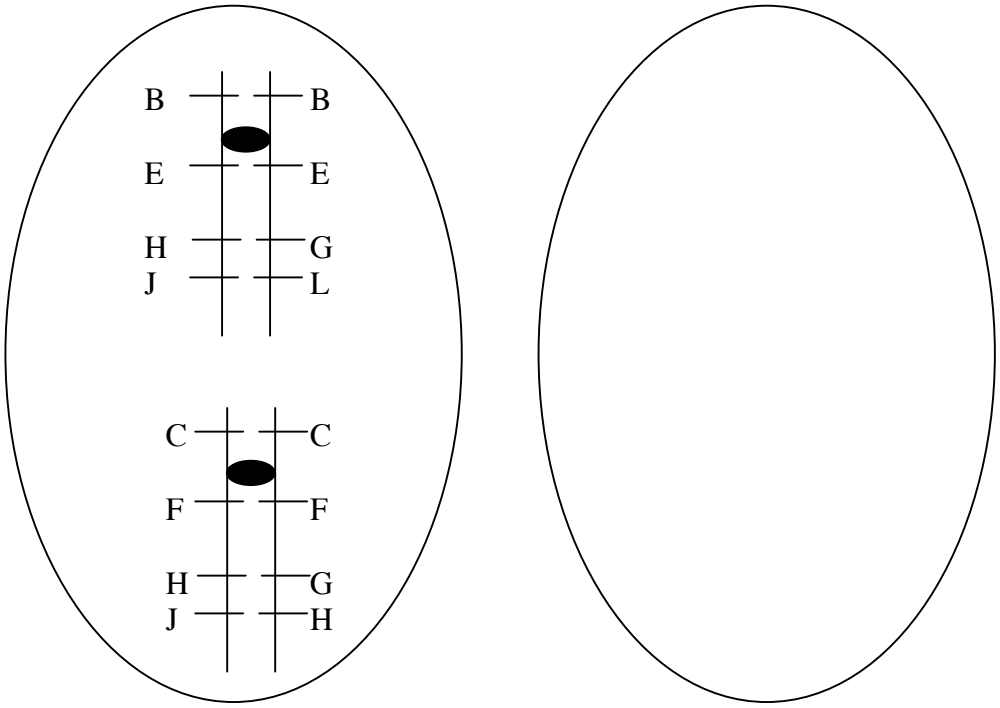

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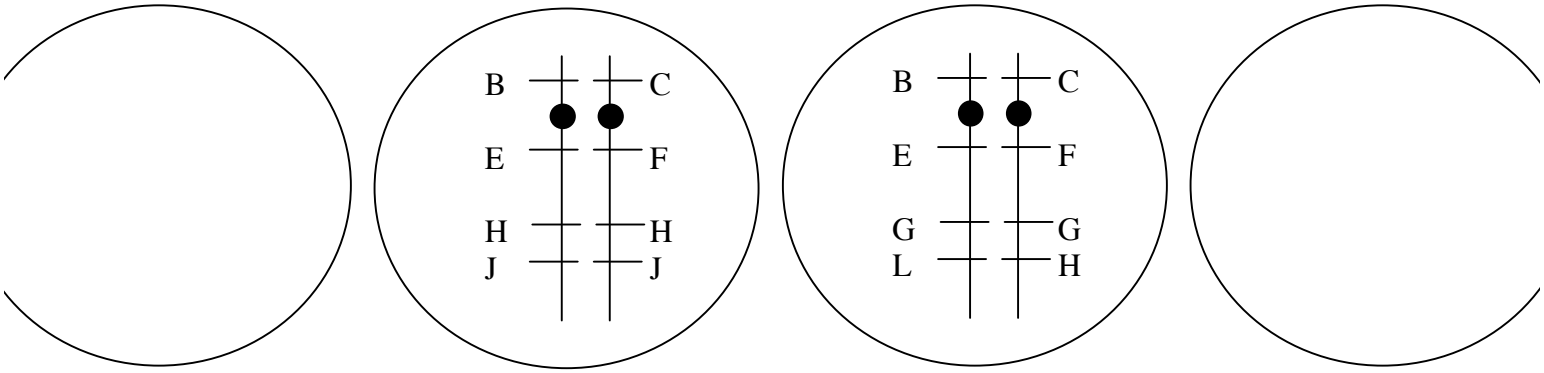

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