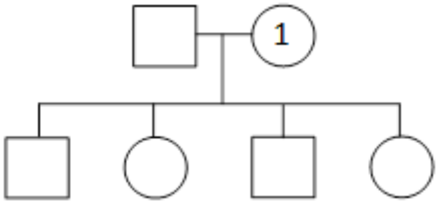
Circle the best single letter choice for each of the following questions before transferring your answers to your computer sheet within the time limit.
Note: *Questions may have 3, 4 or 5 choices.*
Part marks may be allotted for choosing a subset of correct answers.
Choosing any incorrect answer earns a grade of zero on the question.

43 Multiple Choice Questions (1 mark each)

1. Imagine there is an X-chromosome gene that causes Alzheimer's when the protein product is disrupted. Individual #1 has acquired a new recessive synonymous mutation in this gene. How many of their children, shown in the figure, will likely display the disease? Note that squares are males and circles are females.

A. none
B. 1 male only
C. 1 female only
D. 2 males only
E. 2 females only



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2. According to the following complementation table, what is the greatest number of phenotypes caused by disruptions in the same gene?

A. 3
B. 4
C. 6
D. 10

phenotypes	*red*	*navy*	*orange*	*teal*	*purple*	*lime*	*yellow*	*pink*	*aqua*
red	**-**	**+**	**+**	**-**	**+**	**+**	**+**	**+**	**-**
navy		**-**	**-**	**+**	**+**	**-**	**-**	**+**	**+**
orange			**-**	**+**	**+**	**-**	**-**	**+**	**+**
teal				**-**	**+**	**+**	**+**	**+**	**-**
purple					**-**	**+**	**+**	**-**	**+**
lime						**-**	**-**	**+**	**+**
yellow							**-**	**+**	**+**
pink								**-**	**+**
aqua									**-**

---

3. What is the minimal amount of genetic information you need in order to answer the "C-value paradox"?

A. The amount of non-coding DNA in a genome.
B. The amount of protein-coding DNA within a genome.
C. The amount of intron and exon DNA within a genome.
D. All coding and non-coding DNA within a genome.

---

4. What is an evolutionary ratchet?

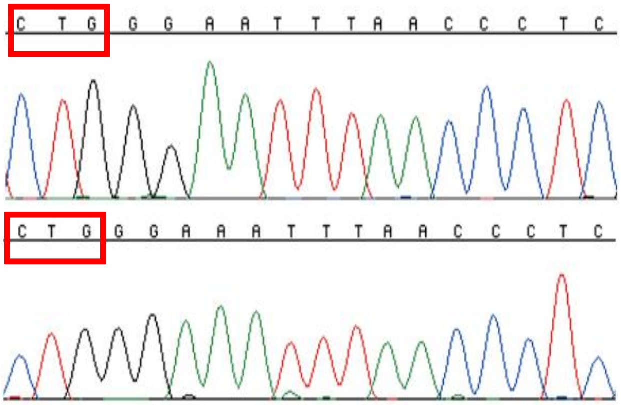
A. The evolution of new alternative splice variants, causing increased phenotypic diversity.
B. When a genetically diverse population undergoes a bottleneck, losing most variation.
C. A single molecule that evolves to perform several discrete, non-overlapping functions.
D. A genetic change increasing biological complexity in a way that is hard to undo.

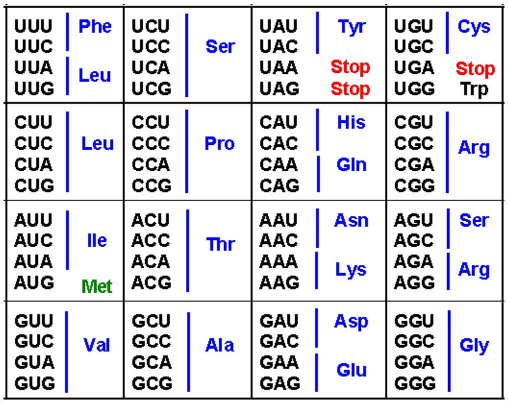
5. Which of the following statements about the APP locus and its effect on Early Onset Familial Alzheimer’s Disease (EOFAD) is true?

   A. All of the known mutations in APP that cause EOFAD are dominant.
   B. Mutations in APP cause EOFAD by affecting its ability to fully function as a secretase.
   C. One type of APP mutation affects the ability of PSEN2 transcripts to bind APP.
   D. All of the known mutations in APP that cause EOFAD affect splicing of its Aβ domain.

---

6. A patient with Early Onset Familial Alzheimer’s Disease (EOFAD) was sequenced for their PSEN2 locus. Their sequencing chromatogram (top) was compared to one from a human without EOFAD (bottom). Both sequences were taken directly from the online human sequence database. The reading frame is shown by the one codon boxed in red. A translation table is given at the right.





UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys
UUC		UCC		UAC		UGC	
UUA	Leu	UCA		UAA	Stop	UGA	Stop
UUG		UCG		UAG	Stop	UGG	Trp
CUU	Leu	CCU	Pro	CAU	His	CGU	Arg
CUC		CCC		CAC		CGC	
CUA		CCA		CAA	Gln	CGA	
CUG		CCG		CAG		CGG	
AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser
AUC		ACC		AAC		AGC	
AUA		ACA		AAA	Lys	AGA	Arg
AUG	Met	ACG		AAG		AGG	
GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly
GUC		GCC		GAC		GGC	
GUA		GCA		GAA	Glu	GGA	
GUG		GCG		GAG		GGG	

What translational consequence occurs due to the above EOFAD patient’s mutation?

A. Missense
B. Nonsense
C. Silent
D. Wobble

---

7. Which of the following statements about evolution is true?

   A. The genome of LUCA was likely RNA and later evolved proteins to perform catalytic functions and DNA for information storage function.
   B. Half of the LECA genome has archaean ancestry, and the other half is alpha-proteobacterian ancestry.
   C. All chloroplasts can be traced back to a single endosymbiotic event between a eukaryote and a cyanobacterium.
   D. Eukaryotic genes with archaean ancestry are more often involved in metabolic functions within the cell.

---

8. Transposase cuts from a:

   A. blunt end cut at the transposon; blunt end cut at the target sequence.
   B. blunt end cut at the transposon; staggered (‘sticky’) cut at the target sequence.
   C. staggered (‘sticky’) cut at the transposon; blunt end cut at the target sequence.
   D. staggered (‘sticky’) cut at the transposon; staggered (‘sticky’) cut at the target sequence.

---

9. A cell has the following genetic compartments: a triploid nucleus with a haploid size of 500kb; one 400kb mitochondria; two identical 200kb mitochondria; two identical 300kb chloroplasts. What is the genome size of this organism?

A. 0.5 Mb
B. 1.4 Mb
C. 1.5 Mb
D. 2.4 Mb
E. 2.9 Mb

---

10. Which of the following functions is not performed by transcriptase?

A. Cutting out the transposable element.
B. Integration of the transposon into the host genome.
C. Cutting the target site in the host genome.
D. Formation of the retrotransposon's RNA intermediate.

---

11. In humans, embryos that are trisomic for the X chromosome develop as females. Duchenne muscular dystrophy is a sex-linked recessive disorder. Consider Rishila, a triple X woman who carries only normal alleles for DMD.

How many copies of the DMD gene are likely being expressed in a given cell during G1 in Rishila's muscles?

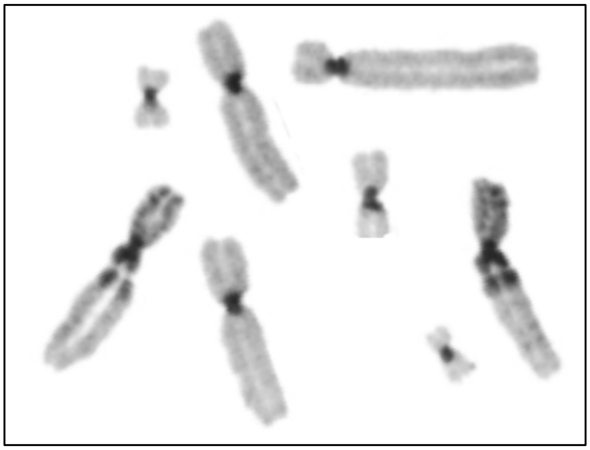
A. 0
B. 1
C. 2
D. 3
E. 6

---

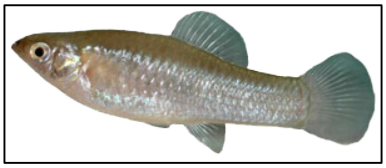
12. The metaphase chromosomes at right were prepared from cancerous white blood cells (leukemia) in a rodent.

Which of the following chromosomal rearrangements is apparent?

A. Translocation
B. Trisomy
C. Inversion
D. Deletion



13. The amazon molly was the first vertebrate to be discovered to reproduce without fertilization. Although molly eggs require the presence of sperm to stimulate their development, no fertilization occurs and no genetic material is contributed to the zygote from sperm. Instead, diploid eggs develop directly into diploid zygotes.



Suppose one of your friends proposed the following hypothesis to explain the origin of these unusual diploid eggs.

"Cells of female amazon mollys prepare for, and enter, the early stages of meiosis as usual. However, at metaphase of meiosis I, the spindle microtubules attach to all kinetochores such that the two sister chromatids of every replicated chromosome are each pulled to opposite poles. (That is, the spindle in meiosis I operates as if it is meiosis II.) The resulting diploid daughter cells function as diploid eggs."

Which of the following predictions is consistent with this hypothesis?

A. Diploid zygotes would all be entirely homozygous.
B. Diploid zygotes would all be different from each other.
C. Diploid zygotes would all have the same genotype, but would be different from their mother.
D. Diploid zygotes would all have the same genotype, that would be the same as their mother.

---

14. *BRCA1* is a tumor suppressor gene. Mutations in this gene are associated with increased risk of cancer, particularly breast cancer. Assume that Marjorie inherited one non-functional *BRAC1* allele from her father and one normal allele from her mother. In her late 20's, Marjorie suffered a mutation in her normal allele with the resulting growth of a tumor. Now cancer free in her 30's, Marjorie has conceived a child.

What is the likelihood that Marjorie has passed a non-functional *BRCA1* allele to her child?

A. 0%
B. 25%
C. 50%
D. 100%
E. Cannot predict because it depends on recombination during meiosis.

---

15. The prefix "hetero" connotes "difference" while "homo" connotes "sameness".

Which of the following statements identifies the particular way in which heteroduplex is "hetero"?

A. Heteroduplex DNA has both backbones from a heterozygote; homoduplex DNA has both backbones from a homozygote.
B. Heteroduplex DNA has backbones with sequences that are not entirely complementary (ie. have mismatches); homoduplex backbone sequences are entirely complementary.
C. Heteroduplex DNA has backbones that are partly recombinant, partly non-recombinant; homoduplex is entirely recombinant or non-recombinant.
D. Heteroduplex DNA has backbones from different chromatids (ie. maternal vs. paternal); homoduplex DNA has both backbones from the same chromatid.

16. Imagine that you are trying to map two genes (*A* and *B*) in fish using recombination frequency. You have acquired two females that you know are heterozygous for both genes (Aa Bb). You test-cross each female to the same homozygous recessive male and get the following distribution of phenotypes among the progeny:

Cross with Female 1	Cross with Female 2
AB – 37	*AB* – 5
ab – 33	*ab* – 4
Ab – 4	*Ab* – 35
aB – 6	*aB* – 36

Which of the following explanations best accounts for drastic difference between the distribution of progeny in these two crosses?

A. The two genes are assorting independently in female 1 but are linked in female 2.
B. The two genes are linked in female 1 and but assorting independently in female 2.
C. The two genes are linked in both females; Female 1 carries both dominant alleles on the same homologue, Female 2 does not.
D. In one female, the genes are linked and less than 50 cM apart; in the other female, the genes are linked but more than 50 cM apart.

---

17. Physical genetic maps, showing the relative location of genes along a chromosome, arise from analysis of genome sequences.

Recombination frequency genetic maps, also showing the relative location of genes along a chromosome, arise through analysis of the progeny distributions generated by test crosses of heterozygotes.

Which of the following statements comparing genetic maps is true?

1. The recombination frequency map for human females would tend to show genes to be further apart than that shown by the recombination frequency map for human males.
2. For genes in the pseudoautosomal region, they would appear to be further apart in the human male recombination frequency map than that shown by the female recombination frequency map.
3. For genes within a paracentric inversion, the recombination frequency map would show them much more tightly linked than shown by the physical map.
4. For antibody genes, physical maps would be different for gametes *vs.* mature B cells.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

---

18. Recall that recombination can be initiated by either a single-strand break or a double-strand break in participating DNA molecules.

    Which of the following is a certain consequence of the initiation of recombination, regardless of whether the initiating event is a single-strand or double-strand break?

    1. gene conversion
    2. Holliday junction
    3. cross-over
    4. heteroduplex DNA

    A. 1, 2 and 3
    B. 1 and 3
    C. 2 and 4
    D. 4 only
    E. All of 1, 2, 3 & 4 are correct.

---

19. The mechanism of action for two chemical mutagens is given below.

Mutagen	Mechanism
Hydroxylamine (HA)	Modifes cytosine to hydroxlaminocytosine, which pairs with adenine.
Ethyl methane sulfonate (EMS)	Modifies guanine to ethylguanine, which pairs with thymine. Modifies thymine to ethylthymine, which pairs with guanine.

Which of the following statements about these mutagens is true?

1. EMS can revert mutations caused by EMS.
2. EMS can revert mutations caused by HA.
3. Both mutagens create transition mutations.
4. HA can revert nonsense mutations.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

---

20. On average, how many *de novo* mutations (not inherited from your parents) are likely present in the nuclear genome of each of your gametes?

    A. 0
    B. 1
    C. 50
    D. 100
    E. 5×10^5

---

21. Chemicals such as ethidium bromide and dioxin are intercalating agents that slide between adjacent bases. They are thought to stabilize the “loops” that form during replication slippage.

Which of the following statements likely applies to this class of mutagens?

1. Such chemicals can revert the same type of mutations that they cause.
2. Such chemicals can cause intragenic suppression of the same type of mutation that they cause.
3. Such chemicals cause frameshift mutations.
4. Such chemicals create SNPs.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

---

22. Imagine that you expose *Drosophila* flies that are homogzygous for the recessive yellow body allele to a mutagen and then cross exposed flies with homozygous recessive mates. Among the progeny you discover a wild type fly.

How could you determine whether the wild type fly arose by reversion or suppression of the yellow body mutation?

1. If the wild type fly has a wild type sequence of the yellow body gene, then the fly must have arisen by reversion.
2. If the wild type fly has neither a wild type gene sequence nor a wild type amino acid sequence, then the fly must have arisen by intergenic suppression.
3. If the wild type fly does not have a wild type gene sequence, but produces a protein from the yellow body gene with a wild type amino acid sequence, then the fly must have arisen by intragenic suppression.
4. If you discover that the mutagen used in your experiment was the same one used to create the original yellow body mutation, then the fly must have arisen by reversion.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

---

23. Which of the following sequences would be the “consensus” sequence derived from the 6 genomes shown at right?

1	AGGAGTT
2	AGCTATT
3	TGCAATA
4	ACGAAAA
5	TCCTAAT
6	TGCAATT

A. T/A G/C G/C T/A G/A T/A
B. Y G C A A T T
C. T/A G C A A T T
D. T/A G G A G T/A
E. T G C A G T T

---

24. The sequence below shows a mutation in the sequence of the tumor suppressor gene TP53. As a result of this change, the protein misfolds and is rapidly recycled in the cytoplasm.

Normal 5′ AATCCGAAGTAGGGCCATTGAAT
Mutant 5′ AATCCGA**T**GTAGGGCCATTGAAT

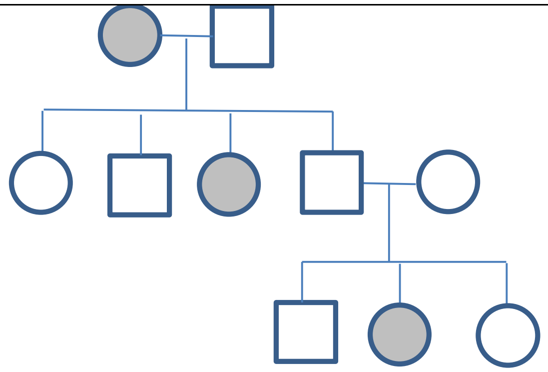
Which of the following statements about this mutation is true?

1. The mutation could be in the 5′ UTR.
2. The resulting phenotype of increased cancer risk would show dominant inheritance.
3. The mutation could be synonymous.
4. The mutation is a transversion.

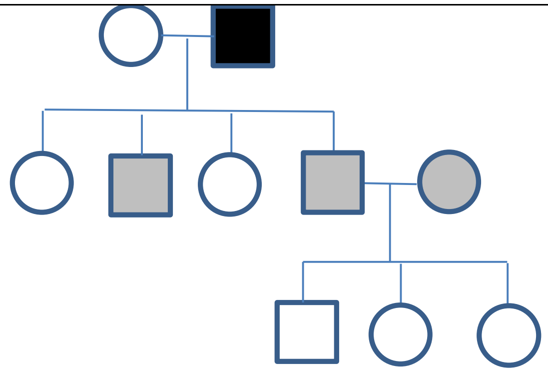
A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

---

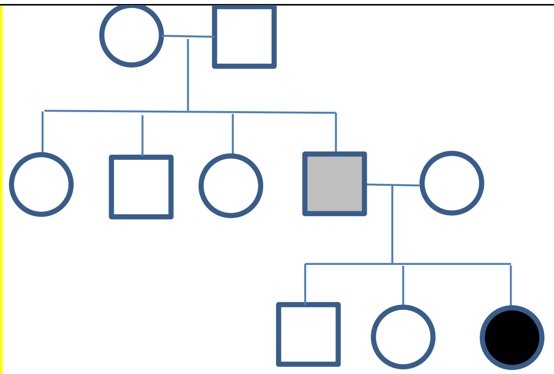
25. If the degree of shading indicates the severity of a trait, which of the following pedigrees illustrates genetic anticipation?



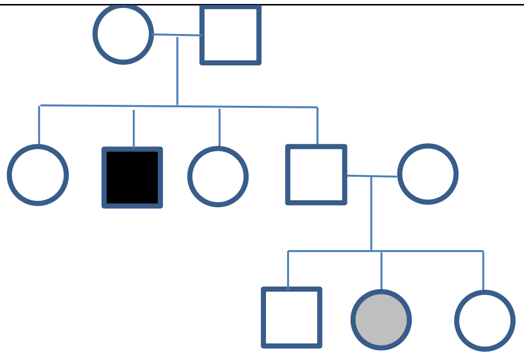
A.



B.



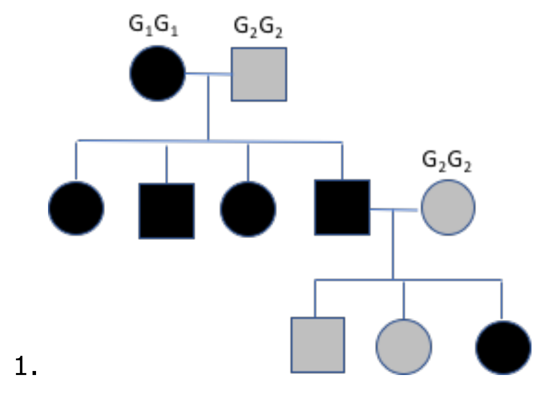
C.



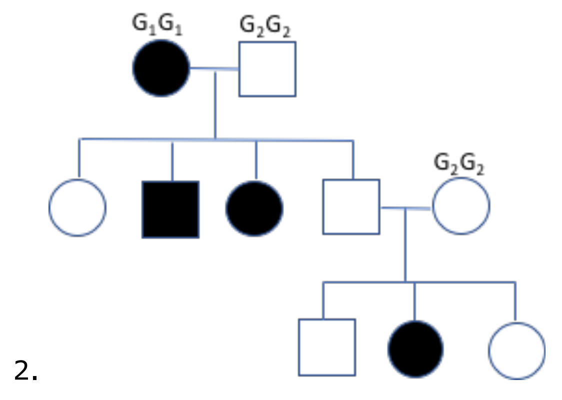
D.

---

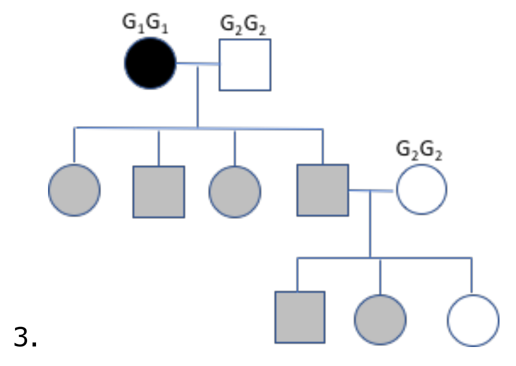
26. If the degree of shading indicates the severity of a trait, which of the following pedigrees illustrates variable expressivity?



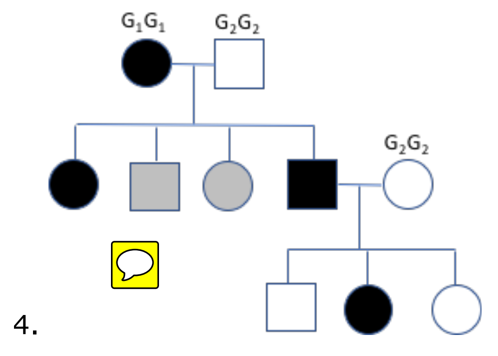
1.



2.



3.



4.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

27. Recall that extensive repeats in the 3′ UTR of a kinase gene mRNA sequester RNA-binding proteins away from splicing reactions, resulting in aberrant processing of other mRNAs which, in turn, results in the characteristic symptoms of myotonic dystrophy.

Which of the following classifications of mutations would apply to this example of expanded triplet repeats?

1. dominant inheritance of disease symptoms
2. polyglutamine disorders
3. gain of function
4. epigenetic marking

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

28. Which of the following statements regarding “pre-mutation” is true?

1. People homozygous for pre-mutations show very mild symptoms of disease.
2. The mechanism responsible for creating pre-mutations is reversible.
3. People heterozygous for pre-mutations show incomplete penetrance.
4. People heterozygous for pre-mutations are at higher risk of having progeny with disease.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

---

29. Short regions of chromosome 1 were sequenced in a population of *Drosophila*. These sequences from three different flies are shown below. Identify the SNP haplotype for Fly #3.

Fly #1: 5′ ATGGCACGAAGCTAAGAATA 3′

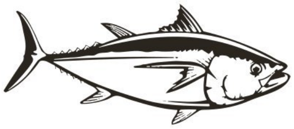
Fly #2: 5′ ATGGCTCGACGCTCATAATA 3′

Fly #3: 5′ ATGGCGCGATGCTAAGAATC 3′

A. 5′-GTAGC-3′
B. 5′-CGATG-3′
C. 5′-GTAGA-3′
D. 5′-CATCG-3′

---

30. “Blue fin” is a species of tuna that is both endangered in the wild and highly prized by sushi chefs. One 450 lb fish recently sold for $4.6 million at auction in Japan.



Imagine that you are about to pay a lot of money for a taste of this famous fish. How could you make use of your knowledge of genetic variation to ensure that the chef is not substituting some other fish in your sushi?

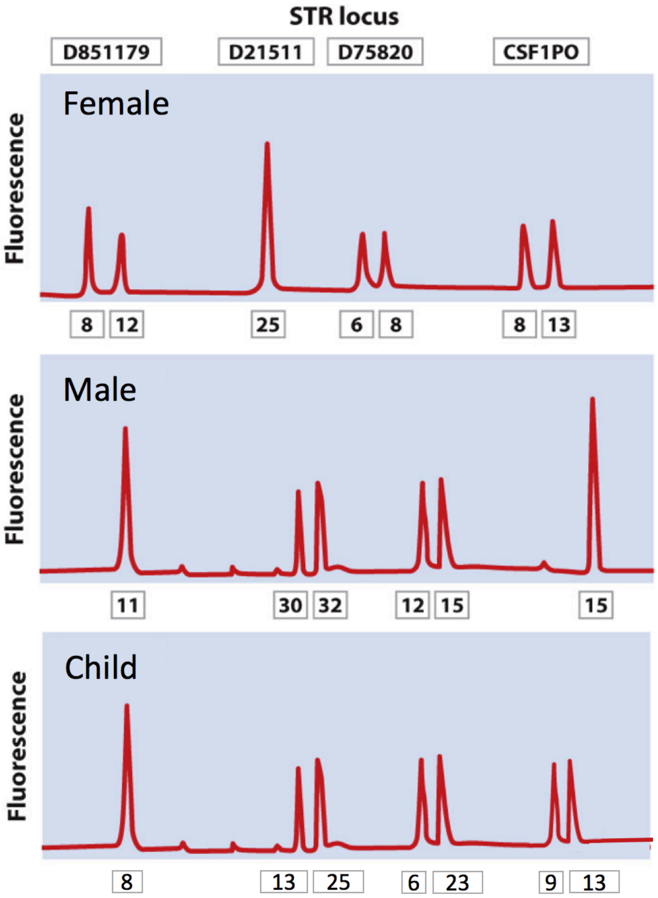
1. You could use genome-wide single nucleotide polymorphism (SNP) haplotyping to confirm that your tuna is part of the famous fish rather than some other blue fin imposter.
2. You could use short tandem repeat (STR) “fingerprints” to confirm that all the pieces of tuna on your plate came from the same animal.
3. You could use DNA barcoding to confirm that the piece of fish you purchased came from a blue fin, and not some other species of tuna.
4. You could use restriction fragment length polymorphisms (RFLP) to confirm that you have been given the choice fatty “toro” cut - obtained from the belly of the fish.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

31. Imagine that two adults, one female and one male, are claiming refugee status at a border crossing. They have a young child who they present as their daughter. While investigating these family relationships, immigration officials obtain the genotypes shown below for four independently assorting STR loci.

Which of the following interpretations is consistent with these data?

A. This child is likely the offspring of these two adults.
B. None of these people is likely related to any of the others.
C. The male and the female are likely brother and sister; they are unrelated to the child.
D. The female is likely the child's mother but the male is not her father.



32. Linkage disequilibrium (LDE) is the tendency of SNPs within a haplotype to be inherited together. Over time, would you expect linkage disequilibrium among such SNPs to be maintained, to increase, or to decrease in human populations?

A. LDE will decrease, because random mutation will generate new SNPs that will give rise to new haplotypes.
B. LDE will increase, because unequal crossing over between SNPs will decrease the physical distance between them.
C. LDE will be maintained, because there is no selective pressure to operating on individual SNPs.
D. LDE will increase, because positive selection will cause the haplotype to become more common.
E. LDE will decrease, because meiotic crossing over will tend to break up the physical linkage among SNPs.

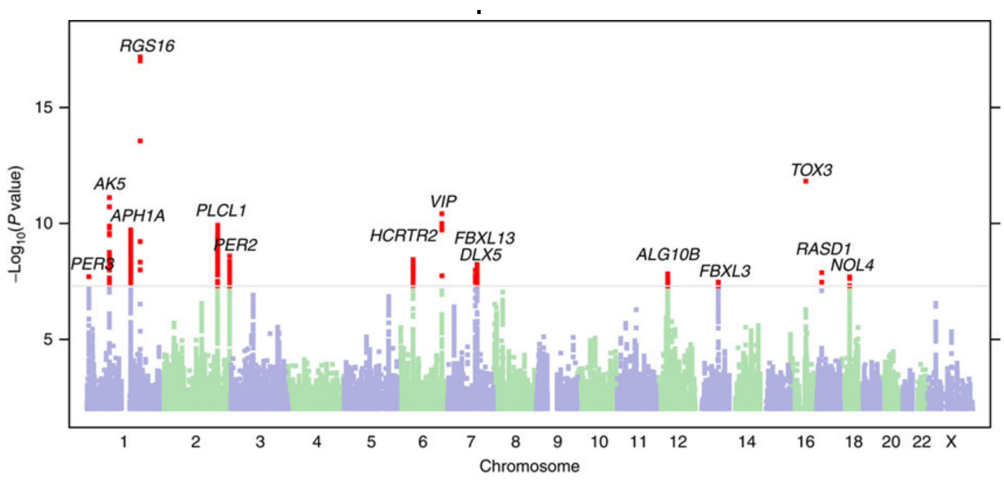
33. Delaki is a young man of African descent who, after taking evolutionary genetics courses, understands that children born to parents who are closely related may show less genetic variability (ie. less heterozygousity) and less resistance to pathogens.

If Delaki wants to maximize the heterozygousity of his children, in which if the following populations should he seek a partner?

A. White European
B. Asian
C. African
D. Indigenous North American

---

34. Genome wide association studies (GWAS) search for relationships between particular SNPs and specific traits. The data are frequently displayed as Manhattan plots, as shown below for the trait of "being a morning person". (I am not making this up.) Note that the Y axis is –Log(P value).

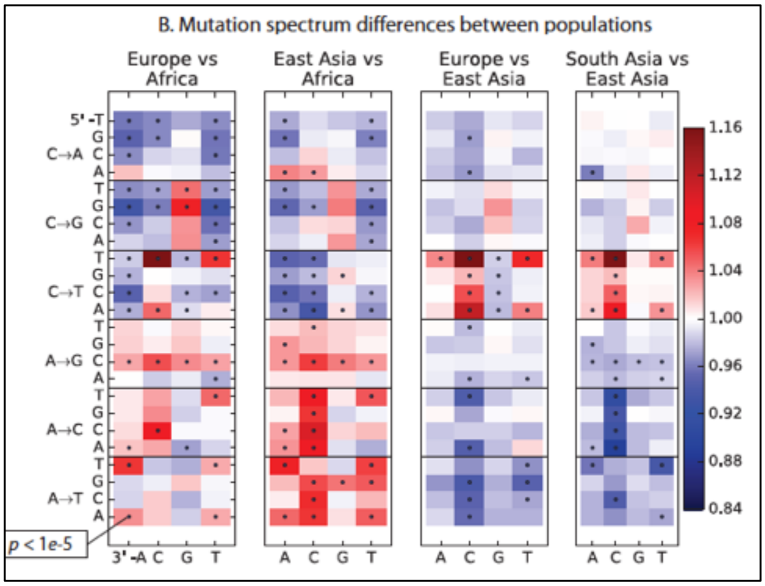


What does it mean for a SNP to plot above the horizontal line (eg. VIP or TOX3)?

A. SNPs plotting above the line show a relationship with the trait that is statistically unlikely to be just due to chance.
B. SNPs plotting above the line are statistically equally likely to be found in people with the trait as people without the trait.
C. SNPs plotting above the line are statistically likely to code for the trait.
D. SNPs plotting above the line show statistically significant genetic linkage with the trait.

---

35. The figure at right is a "heat map" comparing the relative frequency of particular variation in four human populations. (Note that the dots indicate statistical significance.)



Which of the following interpretations of these mutation spectrum differences is correct?

1. East Asians are more similar to South Asians than they are to Africans.
2. The tendency of the sequence 5′TAA to mutate to 5′TTA is very different in both East Asians and Europeans relative to Africans.
3. Taken all together, significant differences in mutation frequency are somewhat more likely to involve mutation of cytosine than adenine.
4. East Asians differ from South Asians most dramatically in transition mutations.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 and 4 are correct

---

36. Karyotype analysis of tumor cells has revealed genomic instability leading to an extremely wide range of chromosomal structural variation.

In which of the following ways is such somatic variation important in cancer biology?

A. Cells with abnormal karyotypes all die by apoptosis, reducing tumor size.
B. Deletion of chromosomal regions can remove proto-oncogenes, leading to excessive cell proliferation.
C. Cells with abnormal chromosome structures will suffer poor pairing and disjunction of homologues during Meiosis I.
D. Cells with abnormal karyotypes may acquire multiple cancer-promoting mutations at the same time.

---

37. Sequencing of tumor genomes has identified "driver" vs. "passenger" mutations.

Which of the following best describes a passenger mutation?

A. Passenger mutations are found in tumor genomes but do not contribute to the tumor phenotype.
B. Passenger mutations are closely linked to driver mutations and tend to be inherited together.
C. Passenger mutations inactivate tumor suppressor genes, resulting in excessive cell growth.
D. Passenger mutations tend to destabilize the genome, resulting in further mutation as cells proliferate.

---

38. Microarrays have limitations for determining gene expression when compared to RNA sequencing (RNA-seq).

Which of the following statements describe a limitation of the microarray approach?

1. Quantification can be difficult on a microarray.
2. Similar sequences may bind to the same microarray probe.
3. Microarrays require prior knowledge of sequences to construct.
4. Microarrays can hybridize only a small number of sequences at a time.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 and 4 are correct

39. Which of the following statements regarding mitotic crossing over is true?

1. Mitotic crossing over can result in loss of heterozygousity in daughter cells.
2. Mitotic crossing over could create a chimeric organism.
3. Mitotic crossing over is likely stimulated by double strand breaks in DNA.
4. Mitotic crossing over could increase diversity in haploid organisms lacking sexual reproduction.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

40. Which of the following statements regarding somatic hypermutation is true?

1. Somatic hypermutation is induced by B-cell activation.
2. Somatic hypermutation introduces uracil into DNA.
3. Somatic hypermutation is dependent upon DNA replication in dividing cells.
4. Somatic hypermutation increases variation in sequences coding for antibody proteins.

A. 1, 2 and 3
B. 1 and 3
C. 2 and 4
D. 4 only
E. All of 1, 2, 3 & 4 are correct.

41. Ataxia telangectasia (ATM) is a human neurodegenerative disorder that is also frequently associated with immune cell cancers and generally weakend immunity. The gene responsible for ATM is associated with double strand break repair.

    Which of the following statements makes a likely connection between ATM and weakend immunity?

    A. The ATM gene is only present in immune cells; mutations that hinder double strand break repair are more severe in these cells.
    B. Generation of antibody and T-cell receptor genes requires creation and repair of double strand breaks in DNA; ATM mutations hinder the repair process.
    C. Double strand breaks occur more frequently in immune cells due to exposure to toxic antigens; ATM mutations hinder the repair process.
    D. The ATM gene is subject to somatic recombination in immune cells. Errors in double strand break repair hinder this process.

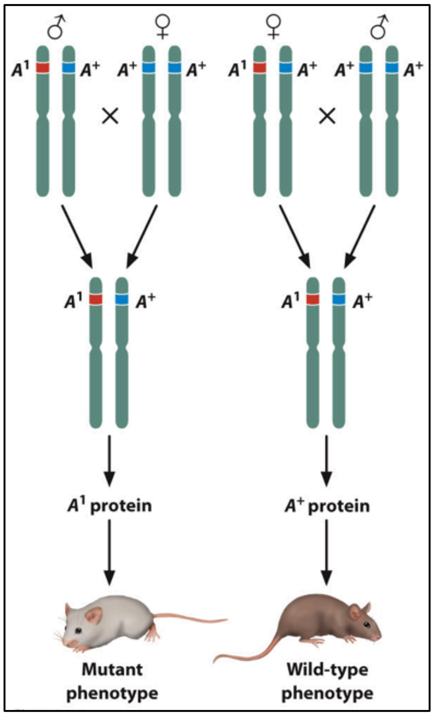
42. Which of the following statements relates to the concept of "genetic conflict"?

    A. The RNA produced by transcription of one gene directly binds to, and inhibits, the RNA transcribed from a different gene.
    B. An insulator sequence blocks the otherwise stimulatory effects of nearby enhancers.
    C. The effect of a mutation in a given gene is reversed by the effect of a different mutation in a different gene.
    D. A trait shown by offspring improves the evolutionary fitness of one parent while decreasing the fitness of the other parent.

43. This figure from the text summarizes a situation in which the allele of the A gene inherited from females is imprinted and nonfunctional. Animals lacking any expression of this gene are not viable.

    Consider a cross involving two heterozygous animals (male A^{1}A^2 x female A$^+$A^1). In this case, the A^2 allele is a "null" allele, making no product at all.

    What fraction of the viable offspring will show the A^1 mutant phenotype?



    A. 1/4
    B. 1/2
    C. 3/4
    D. All